Geriatrics

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Learning Objectives

1. Summarize common age-related pharmacokinetic and pharmacodynamic changes in older adults.
2. Evaluate the pharmacotherapeutic regimens of older adults to support optimal risk and benefit of medications.
3. Assess inappropriate medication prescribing in older adults using accepted tools.
4. Recommend appropriate pharmacotherapy for patients with dementia.
5. Evaluate the risks and benefits of antipsychotic use in older adults with dementia.
6. Recommend appropriate interventions for patients with BPSD (behavioral and psychological symptoms of dementia).
7. Differentiate between the types of urinary incontinence and recommend appropriate treatments.
8. Recommend an appropriate BPH (benign prostatic hypertrophy) treatment, according to the AUASI (American Urological Association Symptom Index).
9. Recommend appropriate analgesic therapy for older adults with osteoarthritis.
10. Discuss the risks and benefits of medication classes used to treat rheumatoid arthritis and associated comorbidities.

Abbreviations in This Chapter

AD  Alzheimer disease
ADLs  Activities of daily living
AUASI  American Urological Association Symptom Index
BPH  Benign prostatic hypertrophy
BPSD  Behavioral and psychological symptoms of dementia
CI  Cholinesterase inhibitor
DMARD  Disease-modifying antirheumatic drug
IADL  Instrumental activities of daily living
LUTS  Lower urinary tract symptoms
MCI  Mild cognitive impairment
MMSE  Mini–Mental State Examination
OA  Osteoarthritis
PSA  Prostate-specific antigen
PVR  Postvoid residual
RA  Rheumatoid arthritis
RF  Rheumatoid factor
TNF  Tumor necrosis factor
UI  Urinary incontinence

Self-Assessment Questions

Answers and explanations to these questions can be found at the end of this chapter.

Questions 1 and 2 pertain to the following case.
An 85-year-old man presents to the primary care clinic after the death of his spouse 1 month earlier. His medical history is significant for hypertension, hyperlipidemia, benign prostatic hypertrophy (BPH), and major depressive disorder. His current medications include lisinopril 10 mg daily, atorvastatin 20 mg daily, tamsulosin 0.4 mg daily, diazepam 5 mg at bedtime as needed for sleep, and escitalopram 10 mg daily. His daughter reports that he has been more lethargic and unsteady walking during the past 3 days. The patient reports trouble sleeping and taking diazepam every night this past week. His blood pressure is 135/72 mm Hg and heart rate is 76 beats/minute. Urinalysis is negative, thyroid-stimulating hormone (TSH) is within the reference range, and Geriatric Depression Scale score is 6/15.

1. Which medication is most contributing to this patient’s lethargy and confusion?
   A. Diazepam.
   B. Lisinopril.
   C. Atorvastatin.
   D. Escitalopram.

2. Which age-related change in pharmacokinetics most likely underlies this patient’s medication-related problem?
   A. Delayed oral absorption.
   B. Decreased renal excretion.
   C. Slowed metabolism in the liver.
   D. Decreased volume of distribution.

Questions 3–5 pertain to the following case.
A 76-year-old woman was recently admitted to a long-term care facility for rehabilitation after several falls at home. Her medical history is significant for hypertension, hypothyroidism, Alzheimer disease (AD), hyperlipidemia, and osteoarthritis (OA). She takes metoprolol succinate 50 mg daily, levothyroxine 75 mcg daily, atorvastatin 10 mg daily, and donepezil 10 mg daily. Her blood pressure is 126/80 mm Hg and heart rate is 66 beats/minute. Basic metabolic panel results are all within reference ranges; 25-hydroxyvitamin D
concentration is 20 ng/mL, TSH is 1.89 mU/L, total cholesterol is 180 mg/dL, low-density lipoprotein cholesterol is 140 mg/dL, high-density lipoprotein cholesterol is 35 mg/dL, and triglycerides is 176 mg/dL. Her Mini-Mental State Examination (MMSE) score is 16/30, and her Geriatric Depression Scale score is 2/15.

3. Which recommendation would be most appropriate to reduce this patient’s risk of falls?
   A. Begin memantine titration.
   B. Initiate vitamin D 1000 units daily.
   C. Decrease metoprolol succinate to 25 mg daily.
   D. Initiate calcium carbonate 500 mg twice daily.

4. Which intervention is best to reduce this patient’s risk of ischemic stroke?
   A. Initiate aspirin 81 mg daily.
   B. Increase atorvastatin to 20 mg daily.
   C. Initiate hydrochlorothiazide 25 mg daily.
   D. Increase metoprolol succinate to 100 mg daily.

5. Which would be most appropriate for the patient’s osteoarthritic knee pain?
   A. Ibuprofen 200 mg four times daily.
   B. Acetaminophen 650 mg three times daily.
   C. Tramadol 50 mg three times daily as needed for pain.
   D. Hydrocodone/acetaminophen 5/325 mg every 4 hours as needed for pain.

Questions 6–8 pertain to the following case.
An 80-year-old woman presents to your clinic accompanied by her daughter, who no longer feels comfortable leaving her mother alone because of her mother’s “increasing forgetfulness.” The patient’s medical history is significant for type 2 diabetes, hypertension, coronary artery disease, congestive heart failure, and OA. She takes the following medications: acetaminophen 650 mg every 6 hours as needed for pain, lisinopril 20 mg daily, furosemide 20 mg daily, potassium chloride 20 mEq daily, carvedilol 12.5 mg twice daily, and glipizide 5 mg daily. Her MMSE score is 18/30. Blood tests obtained last week showed a normal basic metabolic panel, except for a fasting plasma glucose reading of 65 mg/dL. Her hemoglobin A1C (A1C) is 5.6%. A urinalysis is negative. No nutritional deficiencies are noted. The patient’s blood pressure is 130/80 mm Hg and heart rate is 60 beats/minute. She receives a diagnosis of AD.

6. Which initial intervention would be most appropriate to help with this patient’s cognitive function?
   A. Donepezil 10 mg daily.
   B. Galantamine extended release (ER) 24 mg daily.
   C. Memantine 10 mg twice daily.
   D. Rivastigmine patch 4.6 mg daily.

7. Which intervention would be most appropriate to prevent an adverse drug reaction?
   A. Discontinue glipizide.
   B. Discontinue lisinopril.
   C. Reduce carvedilol to 6.25 mg twice daily.
   D. Reduce potassium chloride to 10 mEq daily.

8. One year later, the patient returns to the clinic. She has moved in with her daughter. Lately, she wanders around the house continuously. She often changes clothes, cries out, and asks repetitive questions. Her current medication regimen includes donepezil 10 mg daily, which she has been taking for the past 6 months. Which would be most appropriate for this patient’s new behavioral symptoms?
   A. Initiate olanzapine 5 mg daily.
   B. Initiate risperidone 0.5 mg twice daily.
   C. Change the donepezil dosage to 23 mg daily.
   D. Change acetaminophen to 650 mg every 6 hours around-the-clock.

9. An 80-year-old woman had a total right knee replacement 3 days ago after conservative strategies for OA failed. Her medical history is significant for hypothyroidism, OA, and hyperlipidemia. Her current medications include simvastatin 20 mg daily, risedronate 35 mg weekly, levothyroxine 75 mcg daily, and oxycodone/acetaminophen 5/325 mg 1 tablet every 4 hours as needed for moderate pain. She is in the hospital preparing for discharge. As the pharmacist is counseling the patient on her discharge medication, the patient reports a new onset of “losing her water” the day before and again overnight. Which intervention would be most appropriate for this patient?
A. Urinalysis.  
B. Pelvic floor exercises.  
C. Tolterodine 2 mg daily.  
D. Duloxetine 20 mg daily.

Questions 10 and 11 pertain to the following case.  
A 69-year-old man with hypertension and BPH is admitted to the hospital after a motorcycle collision. He had serious injuries resulting in a left leg above-the-knee amputation and has undergone several surgical procedures and rehabilitation in the past 2 weeks. His current medications include tamsulosin 0.4 mg daily, atenolol 25 mg daily, amlodipine 10 mg daily, senna/docusate 8.6/50 mg twice daily, oxycodone controlled release 10 mg every 12 hours, and hydromorphone 4 mg every 3 hours as needed for breakthrough pain (uses 1–2 daily). His blood pressure is 155/88 mm Hg, heart rate is 84 beats/minute, and postvoid residual (PVR) volume is 400 mL after voiding 110 mL. His chronic medical conditions are unremarkable except for hypertension, BPH, and gastroesophageal reflux disease.

10. Which intervention would be most appropriate for this patient?  
A. Change tamsulosin to alfuzosin 10 mg once daily.  
B. Increase atenolol to 50 mg daily.  
C. Change tamsulosin to terazosin 5 mg daily.  
D. Reduce hydromorphone to 2 mg every 3 hours as needed for breakthrough pain.

11. One year later, the patient has OA of his right knee. His current medications are amlodipine 10 mg daily, acetaminophen 1000 mg three times daily, omeprazole 40 mg daily, and aspirin 81 mg daily, together with treatment for his BPH. Which agent would be best to initiate for this patient’s knee pain?  
A. Celecoxib 200 mg daily  
B. Naproxen 500 mg twice daily  
C. Diclofenac 1% gel apply 4 g to knee every 6 hours.  
D. Methylprednisolone 40 mg injected into affected joint.

Questions 12 and 13 pertain to the following case.  
A 72-year-old woman (height 66 inches, weight 82 kg) whose medical history is significant for rheumatoid arthritis (RA), type 2 diabetes, gastroesophageal reflux disease, and hypothyroidism presents to the clinic with inflammation of the joints of the hands and stiffness lasting 1–2 hours in the morning. She is a smoker. Her current medications include pantoprazole 40 mg daily, metformin 850 mg twice daily, levothyroxine 100 mcg daily, folic acid 1 mg daily, methotrexate 12.5 mg weekly, naproxen 500 mg twice daily, calcium 600 mg twice daily, and vitamin D 1000 units twice daily. Her laboratory tests show a negative rheumatoid factor (RF) but positive anti–cyclic citrullinated peptides. The physician determines that this is a flare of moderate disease.

12. Which would be the most appropriate intervention for maintenance treatment of this patient’s RA?  
A. Change naproxen to prednisone 20 mg daily.  
B. Change methotrexate to 25 mg intramuscularly.  
C. Change methotrexate to leflunomide 20 mg daily.  
D. Add sulfasalazine 500 mg twice daily and hydroxychloroquine 400 mg daily.

13. Three months later, the patient has responded to therapy. Her latest bone densitometry scan shows a bone mineral density T-score of –2.0. Her vitamin D concentration is 40 ng/mL. Which recommendation would be most appropriate to help reduce the patient’s risk of major osteoporotic fractures?  
A. Give raloxifene 60 mg daily.  
B. Give risedronate 35 mg weekly.  
C. Give teriparatide 20 mcg subcutaneously daily.  
D. Increase to calcium 600 mg and vitamin D 2000 mg twice daily.
BPS Pharmacotherapy Specialty Examination Content Outline
This chapter covers the following sections of the Pharmacotherapy Specialty Examination Content Outline:

1. Domain 1: Patient–specific Pharmacotherapy
   a. Tasks 1a, 1b, 2a, 2b, 2c, 3a, 3b, 3c, 3d, 4a, 4b, 4c, 4d, 6a and 6b
   b. Systems and Patient-Care Problems:
      i. Dementia
      ii. Behavioral Symptoms of Dementia
      iii. Urinary Incontinence
      iv. Benign Prostatic Hypertrophy
      v. Arthritis
      vi. Osteoarthritis and Rheumatoid Arthritis
I. OPTIMIZING PHARMACOTHERAPY IN OLDER ADULTS

A. Aging
1. Aging is a normal process whereby the human body declines after peak growth and development. In general, aging results as the body responds to environmental stressors according to the person’s health and lifestyle factors together with genetic makeup. If environmental stressors are severe enough or individual factors have too small a reserve capacity, aging causes frailty, disability, and increased vulnerability to disease and death.
2. At present, 13.3% (2010 U.S. Census) of Americans are 65 years or older. This figure is projected to rise to 20% by 2050. Older adults constitute about 13% of the population, but they are responsible for:
   a. 34% of medication costs
   b. 36% of hospital stays
   c. 40% of medication-related hospitalizations
   d. 50% of medication-related deaths
3. At least $30 billion/year is spent on medication-related morbidity.
4. There is large heterogeneity in older adults: Diversity is increasing, and incomes have a wide range; some people live independently into their 90s and beyond, whereas others become frail and dependent at a younger age. Measurement of aging with years of life is insensitive to the differences between older adults.
   a. If an individual survives to age 65, he or she will likely live an additional 13–20 years.
   b. If an individual survives to age 85, he or she will likely live an additional 6–7 years.

B. Pharmacokinetic Changes Associated with Aging
1. Common physiologic changes occur in most older adults, but they are highly variable because of differences in genetics, lifestyle, and environment.

Table 1. Common Physiologic Changes with Age That May Change Drug Pharmacokinetics

<table>
<thead>
<tr>
<th>Organ System</th>
<th>Physiologic Change with Aging</th>
<th>Effect on Pharmacokinetics</th>
</tr>
</thead>
<tbody>
<tr>
<td>GI</td>
<td>Or no change in stomach pH</td>
<td>• ▼ Absorption of some drugs and nutrients requiring acid environment</td>
</tr>
<tr>
<td></td>
<td>GI blood flow</td>
<td>• ▼ Absorption rate may be prolonged</td>
</tr>
<tr>
<td></td>
<td>Slowed gastric emptying</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Slowed GI transit</td>
<td></td>
</tr>
<tr>
<td>Skin</td>
<td>Thinning of dermis</td>
<td>• ▼ Or no change to drug reservoir formation with transdermal formulation</td>
</tr>
<tr>
<td></td>
<td>Loss of subcutaneous fat</td>
<td></td>
</tr>
<tr>
<td>Body composition</td>
<td>▼ Total body water</td>
<td>• ▼ Volume of distribution and accumulation of lipid-soluble drugs</td>
</tr>
<tr>
<td></td>
<td>▼ Lean body mass</td>
<td>• ▼ Volume of distribution of water-soluble drugs</td>
</tr>
<tr>
<td></td>
<td>▼ Body fat</td>
<td>• ▼ Free fraction of highly protein-bound drugs</td>
</tr>
<tr>
<td></td>
<td>▼ Or unchanged serum albumin</td>
<td></td>
</tr>
<tr>
<td></td>
<td>▼ α1-Acid glycoprotein</td>
<td></td>
</tr>
<tr>
<td>Liver</td>
<td>▼ Liver mass</td>
<td>• ▼ First-pass extraction and metabolism</td>
</tr>
<tr>
<td></td>
<td>▼ Blood flow to the liver</td>
<td>• ▼ Half-life and</td>
</tr>
<tr>
<td></td>
<td>▼ Or no change in CYP enzymes</td>
<td>• ▼ Clearance of drugs with a high first-pass extraction and metabolism</td>
</tr>
<tr>
<td>Renal</td>
<td>▼ GFR</td>
<td>• ▼ Or no change in phase I metabolism</td>
</tr>
<tr>
<td></td>
<td>▼ Renal blood flow</td>
<td>• ▼ No change in phase II drug metabolism</td>
</tr>
<tr>
<td></td>
<td>▼ Tubular secretion</td>
<td></td>
</tr>
<tr>
<td></td>
<td>▼ Renal mass</td>
<td></td>
</tr>
</tbody>
</table>

CYP = cytochrome P450; GFR = glomerular filtration rate; GI = gastrointestinal.
2. Absorption
   a. Iron, vitamin B_{12}, antifungals, and calcium are decreased with hypochlorhydria or achlorhydria.
   b. Slower gastric emptying may increase the risk of ulceration from aspirin, nonsteroidal anti-inflammatory drugs (NSAIDs), bisphosphonates, or potassium chloride tablets.
   c. Most drugs are absorbed by passive diffusion without significant age-related changes.
   d. Transdermal formulations usually require a subcutaneous fat layer to form a drug reservoir for absorption. Use with caution in patients who are thin or cachetic.
3. Distribution
   a. Lipid-soluble benzodiazepines such as diazepam have an increased half-life in older adults.
   b. Highly albumin-bound drugs such as phenytoin may have a larger fraction of free (active) drug.
   c. P-glycoprotein, an efflux transporter for several organs including the brain, decreases with aging, which may lead to higher brain concentrations of medications. One example is opioid analgesics.
4. Metabolism
   a. Morphine and propranolol clearance are substantially reduced because of a reduction in first-pass metabolism. Expect other drugs with high first-pass metabolism to be affected similarly.
   b. Changes in metabolism through phase I (oxidative) and cytochrome P450 (CYP) enzymes are variable and confounded by age, sex, concomitant drugs, and genetics.
   c. Lorazepam, oxazepam, and temazepam depend on phase II metabolism and are less affected by age-related changes in metabolism.
5. Elimination
   a. Drugs eliminated through glomerular filtration must be dosed according to individual estimated renal function. Chronic medication examples can be found in the 2019 American Geriatrics Society (AGS) Beers Criteria.
   b. The Cockcroft-Gault equation is a validated method to estimate creatinine clearance (CrCl) for drug dosing in older adults.
   c. The National Kidney Foundation recommends using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) Creatinine Equation (2009) to estimate glomerular filtration rate. However, this recommendation has not been validated in older adults.

Table 2. Differences in Renal Estimation with Common Formulas

<table>
<thead>
<tr>
<th>Patient: 85-year-old person with an SCr of 1 mg/dL</th>
<th>Cockcroft-Gault CrCl (mL/min/1.73 m^{2})</th>
<th>MDRD Estimated GFR (mL/min/1.73 m^{2})</th>
<th>CKD-EPI CrCl (mL/min/1.73 m^{2})</th>
</tr>
</thead>
<tbody>
<tr>
<td>64-inch-tall white woman weighing 60 kg</td>
<td>39</td>
<td>56</td>
<td>51 (stage 3)</td>
</tr>
<tr>
<td>64-inch-tall African American woman weighing 60 kg</td>
<td>39</td>
<td>68</td>
<td>60 (stage 2)</td>
</tr>
<tr>
<td>70-inch-tall white man weighing 75 kg</td>
<td>57</td>
<td>75</td>
<td>68 (stage 2)</td>
</tr>
<tr>
<td>70-inch-tall African American man weighing 75 kg</td>
<td>57</td>
<td>91</td>
<td>79 (stage 2)</td>
</tr>
</tbody>
</table>

Cockcroft-Gault: CrCl = [(140 – age) × weight in kg]/[(72 × SCr)] × 0.85 if female (use actual weight if it is less than ideal body weight)

MDRD: Estimated GFR = 186 × SCr × 1.154 × age − 0.203 × 1.21 if black × 0.742 if female

CKD-EPI Creatinine Equation 2009*: CKD-EPI equation expressed as a single equation: GFR = 141 × [min(SCr/κ, 1)]^a × max(SCr/κ, 1) − 1.209 × age − 0.993] × 1.018 (if female) × 1.159 (if African American)

*SCr is standardized SCr in milligrams per deciliter; x is 0.7 for women and 0.9 for men, α is −0.329 for women and −0.411 for men, min indicates the minimum of SCr/κ or 1, and max indicates the maximum of SCr/κ or 1.

CKD-EPI = Chronic Kidney Disease Epidemiology Collaboration; CrCl = creatinine clearance; MDRD = Modification of Diet in Renal Disease.
d. Some clinicians round the serum creatinine concentration (SCr) up to 1 mg/dL because older adults have lower muscle mass, which produces less creatinine, and an extremely low SCr would over-estimate renal function with these formulas. This rounding is not supported by evidence and remains controversial. In addition, clinicians may use adjusted weight for patients with obesity with formulas used for younger adults, though evidence in older adults is lacking.

C. Pharmacodynamic Changes Common with Aging

1. Increased sensitivity
   a. Benzodiazepines and opioids: Increased sensitivity to the central nervous system (CNS) effects
   b. Antipsychotics, metoclopramide: Extrapyramidal effects and tardive dyskinesia
   c. Tricyclic antidepressants, α-blockers, antihypertensives: Orthostatic hypotension
   d. Warfarin: Greater inhibition of synthesis of vitamin K–dependent clotting factors; increased risk of bleeding
   e. NSAIDs: Gastrointestinal (GI) bleeding
   f. Anticholinergic agents: Increased risk of confusion, dry mouth, constipation, other adverse effects

2. Decreased sensitivity
   a. β-Blockers
   b. β-Agonists

3. Impaired homeostasis
   a. Diuretics, angiotensin-converting enzyme inhibitors: Sodium and electrolytes
   b. Diuretics: Hydration status

**Patient Case**

*Questions 1 and 2 pertain to the following case.*

An 85-year-old woman (weight 65 kg) who resides at home with her daughter has a medical history significant for type 2 diabetes and hypertension, and 1 year ago, she had a right hip fracture after a fall. Her regularly scheduled medications include glyburide 10 mg daily, lisinopril 10 mg daily, metformin 500 mg twice daily, aspirin 81 mg daily, and a multivitamin daily. Her as-needed medications include melatonin 6 mg at bedtime as needed for sleep, meclizine 25 mg ½ tablet three times daily as needed for dizziness, and docusate 100 mg twice daily. Her laboratory results show fasting plasma glucose 90 mg/dL, sodium (Na) 138 mEq/L, potassium (K) 4.5 mEq/L, chloride (Cl) 102 mEq/L, carbon dioxide (CO₂) 25 mEq/L, blood urea nitrogen (BUN) 30 mg/dL, SCr 1.8 mg/dL, and TSH 4.0 mU/L.

1. Considering the potential for altered pharmacokinetics, which set of medications is most likely to cause problems for the patient?
   A. Aspirin and melatonin.
   B. Lisinopril and meclizine.
   C. Lisinopril and metformin.
   D. Glyburide and metformin.

2. Considering the potential for increased pharmacodynamic sensitivity, which set of medications is most likely to cause problems for the patient?
   A. Aspirin and melatonin.
   B. Lisinopril and meclizine.
   C. Lisinopril and metformin.
   D. Glyburide and metformin.
D. Optimal Pharmacotherapy in Older Adults
   1. In an optimal pharmacotherapeutic regimen, the benefit of the therapy outweighs the risk of adverse effects.
   2. To reduce risk, doses of many medications must be adjusted in older adults because of age-associated changes in drug pharmacokinetics and pharmacodynamics.
   3. Alternative medications may be more appropriate because of these changes.
   4. Therapeutic window becomes smaller even with dose and drug adjustments.

E. Drug-Related Assessment for Risk in Older Adults
   1. Overuse of medications
      a. Unnecessary drugs: Use of more medications than clinically indicated and unneeded therapeutic duplication
      b. Common unnecessary drugs: GI agents, CNS agents, vitamins, minerals
      c. May be caused by
         i. Prescribing cascade: When a drug is prescribed for treating another drug’s adverse effects
         ii. Several prescribers
         iii. Care transitions
   2. Underuse of medications
      a. Omitted but necessary or indicated drug therapy or inadequate dosing
      b. Commonly underused drugs: Anticoagulants, statins, antihypertensives
      c. Medications considered appropriate according to guidelines may be omitted because prescriber or patient is overly wary of adverse drug effects.
   3. Nonadherence
      a. Unintentional nonadherence caused by complex drug regimen
      b. Dementia or other cognitive impairment increases risk.
      c. Cost of medications is another barrier.
      d. Intentional nonadherence because of patient health beliefs or concerns
   4. Withdrawal syndromes
      a. Abrupt discontinuation of medication may cause rebound symptoms or delirium.
      b. Common culprits: Antihypertensives, antidepressants, anxiolytics, pain medications
   5. Inappropriate medications
      a. Explicit tools commonly used to identify for quality measures. Best known is the AGS Beers Criteria for Potentially Inappropriate Medications. Alternative medications to the potentially inappropriate agents listed in this guideline are also available from AGS.
         i. Evidence-based list of drugs likely to cause problems
         ii. Adopted by many federal agencies and Part D plans
         iii. Arranged as drugs and drug classes to avoid, drugs to avoid in certain diseases or conditions, and drugs to be used with caution
         iv. Examples: Anticholinergics, benzodiazepines, sedative-hypnotics, older antipsychotics, certain opiates or pain medications, hypoglycemics, NSAIDs, and GI drugs
      b. Implicit tools are patient-centered, take more time to apply. Best studied is the Medication Appropriateness Index.
         i. 10 questions to ask about each medication regarding indication, effect, dosing, directions, interactions, duration, and cost
         ii. Indication, effectiveness, and correct dosage carry the most weight.
6. Choosing Wisely criteria
   a. 10 things to question in older adults
   b. 7 of the 10 items are drug related.
      i. Antipsychotics in patients with dementia should be avoided.
      ii. Target A1C in diabetes management is 7.5% or higher.
      iii. Avoid benzodiazepines and sedative-hypnotics for insomnia, agitation, or delirium.
      iv. Do not initiate antimicrobials for bacteriuria without symptoms.
      v. Assess benefit-risk of cholinesterase inhibitors (CIs).
      vi. Appetite stimulants are not helpful for anorexia or cachexia.
      vii. Drug regimen review is necessary with every new prescription.

Patient Case
Questions 3–5 pertain to the following case.
A 70-year-old woman (height 66 inches, weight 71.7 kg [158 lb]) is in the clinic for an evaluation by the clinical pharmacist for polypharmacy. She has complaints of fatigue, light-headedness, constipation, and “too many medicines.” Her medical history is significant for hypertension, coronary artery disease (drug-eluting stent 8 years ago), chronic obstructive pulmonary disease, diabetes mellitus, incontinence, frequent urinary tract infections, depression, and moderate dementia. Vital signs include blood pressure 160/82 mm Hg, heart rate 51 beats/minute, respiratory rate 16 breaths/minute, and oxygen saturation 99% on room air. Her current medications are as follows: fluticasone/salmeterol 250/50 1 puff twice daily, aspirin 81 mg daily, acetaminophen 650 mg three times daily, clopidogrel 75 mg daily, donepezil 10 mg daily, glipizide 5 mg twice daily, lisinopril 10 mg daily, loratadine 10 mg daily, metoprolol 50 mg twice daily, paroxetine 50 mg daily, ranitidine 150 mg twice daily, simvastatin 40 mg at bedtime, and tolterodine 2 mg at bedtime. Nitrofurantoin 50 mg twice daily for 10 days was initiated 3 days ago. Laboratory values from her physician visit 3 days before are as follows: Na 130 mg/dL, K 4.2 mEq/dL, Cl 99 mg/dL, CO2 24 mEq/dL, BUN 24 mg/dL, SCr 1.6 mg/dL, fasting glucose 67 mg/dL, A1C 6.3%, urinalysis negative except for blood- small, pH 7.5, RBC 11–25/high-power field (HPF), white blood cells 0–2/HPF, and bacteria 168/HPF.

3. Which medication list best depicts the medications with the greatest potential to harm this patient, according to the AGS 2015 Beers Criteria?
   A. Paroxetine, ranitidine, donepezil, tolterodine.
   B. Donepezil, metoprolol, glipizide, simvastatin.
   C. Glipizide, donepezil, nitrofurantoin.
   D. Metoprolol, clopidogrel, ranitidine.

4. Given the available patient information, which set of medications is least appropriate for this patient, according to the Medication Appropriateness Index?
   A. Fluticasone/salmeterol, ranitidine, donepezil, tolterodine.
   B. Metoprolol, clopidogrel, ranitidine.
   C. Aspirin, glipizide, donepezil, nitrofurantoin.
   D. Paroxetine, nitrofurantoin, simvastatin.

5. Which medications would best be discontinued, according to the Choosing Wisely criteria?
   A. Paroxetine, ranitidine, donepezil, tolterodine.
   B. Metoprolol, clopidogrel, ranitidine.
   C. Glipizide, donepezil, nitrofurantoin.
   D. Ranitidine, nitrofurantoin, glipizide, tolterodine.
F. Changes in Function Associated with Aging
   1. Quality of life, place of residence, and social and physical function may become more important than duration of life.
   2. Instrumental activities of daily living (IADLs)
      a. Examples: Doing housekeeping, using telephone, managing medications, shopping, cooking, managing money
      b. Need to do these to live independently
   3. Activities of daily living (ADLs)
      a. Examples: Feeding, dressing, bathing, toileting, transferring
      b. Nursing home or home caregivers are required if ADLs cannot be performed.
   4. Cognitive screening
      a. MMSE
      b. Montreal Cognitive Assessment
      c. SLUMS (St. Louis University Mental Status) examination
   5. Mood: Geriatric Depression Scale
   7. Drugs can alter cognition, mood, and mobility.

G. Geriatric Syndromes
   1. Geriatric syndromes follow a concentric model, with many risk factors and several etiologies contributing to a clinical presentation rather than the linear model with one etiology following a defined pathogenesis.
   2. Falls
      a. Possible etiologies: Psychoactive medications, polypharmacy, orthostatic hypotension, hypoglycemia, hyponatremia, myocardial infarction, urinary tract infection
      b. Examples of contributing risk factors: Vitamin D deficiency, poor balance, deconditioning/muscle weakness, poor vision, environment
      c. STEADI falls program, available from the CDC (https://www.cdc.gov/steadi/index.html), contains materials for patients and providers to improve awareness and mitigate risk.
   3. Delirium
      a. Possible etiologies: Psychoactive medications, polypharmacy, hypoglycemia, hyponatremia, myocardial infarction, urinary tract infection
      b. Example of contributing risk factors: Dementia, stroke, vitamin B₁₂ deficiency, poor hearing, lack of sleep
   4. Hazards of hospitalization
      a. Usual aging involves a decline in several organ systems, which are further compromised when an older patient is admitted to the hospital and expected to remain in bed.
         i. Immobilization leads to deconditioning. Regaining what was lost takes longer in older adults.
         ii. Immobilization and inability to obtain water lead to decreased plasma volume, which can lead to syncope, falls, and fractures.
         iii. Sensory deprivation from isolation and lack of glasses or hearing aids can lead to delirium, which may be treated with restraints or antipsychotics.
         iv. Immobilization and “tethers” (e.g., intravenous lines, oxygen lines, catheters) necessitate nursing assistance to bathroom. Unavoidable delay may lead to incontinence, catheters, infections, falls, and pressure sores.
         v. Prescribed diets or nothing-by-mouth status leads to dehydration, malnutrition, insertion of feeding tubes, and aspiration pneumonia.
      b. Preventable adverse drug events are common contributors to increased morbidity and mortality in older hospitalized adults.
c. Functional decline typically follows a hospitalization and is called a “cascade to dependency.”

d. One study showed that subjects with a loss of ADLs at discharge had a higher mortality rate (40% at 12 months), with only 30% returning to baseline function.

e. Early mobility, adequate nutrition, reduced polypharmacy, and early discharge planning may reduce functional disability and length of stay.

### Patient Case

**Questions 6 and 7 pertain to the following case.**

A 70-year-old woman is admitted to the hospital with a broken arm after a fall. While in the hospital, she is on bedrest most of the time, loses 2 kg (current weight 63 kg), and has trouble sleeping. She is to be discharged to a rehabilitation facility for 2–3 weeks of therapy. Her medications at discharge are glipizide 5 mg daily, lisinopril 10 mg daily, aspirin 81 mg daily, a multivitamin daily, mirtazapine 15 mg at bedtime, calcium 500 mg twice daily, and tramadol 25 mg every 8 hours as needed for pain.

6. When recommending medication changes for this patient, which functional assessment is most important to evaluate?
   A. IADLs.
   B. Depression.
   C. Pressure sores.
   D. Gait and balance.

7. To maintain and improve function in this patient, which intervention is best to implement?
   A. Add simvastatin 10 mg daily.
   B. Increase lisinopril to 20 mg daily.
   C. Add vitamin D 1000 units twice daily.
   D. Change tramadol to naproxen 500 mg twice daily as needed for pain.

### II. DEMENTIA

A. Epidemiology
   1. Affects 4–5 million people in the United States
   2. Of people 65 years and older, 6% have dementia, increasing to 30%–50% of those 85 years and older.

B. Dementia Definition: Cognitive decline in complex attention, executive function, learning and memory, language, and/or perceptual–motor or social cognition AND interferes with work or social functions
   1. Delirium should be ruled out first.
      a. Delirium: A disturbance in attention and awareness developing over hours to days with fluctuation during the day
      b. Delirium is a geriatric syndrome, with age, underlying dementia, functional impairment, and medical comorbidities as risk factors.
      c. Etiologies include medications such as sedative-hypnotics, antidepressants, anticholinergics, opioids, anticonvulsants, and antiparkinson drugs.
   2. *Mild cognitive impairment* (MCI) is a term used to describe the condition of people with some deficits in cognition who do not meet the criteria for dementia.
   3. AD is the most common type of dementia.
   4. Theories of pathogenesis include cholinergic, β-amyloid plaques, tau protein (neurofibrillary tangles), genetics (apolipoprotein E4), and inflammation (cytokines, prion).
5. Several other types of dementia exist; few are reversible.

Table 3. Comparisons of Memory Impairment and Dementias with AD

<table>
<thead>
<tr>
<th>Disease</th>
<th>Differences from AD</th>
<th>Treatment Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td><strong>Common Irreversible Causes</strong></td>
</tr>
<tr>
<td>MCI</td>
<td>No interference with work or social functions</td>
<td>Eliminate or control risk factors for dementia</td>
</tr>
<tr>
<td></td>
<td>1 in 5 progress to AD</td>
<td>May use Cls, which reduced risk of progression by 40% in one study</td>
</tr>
<tr>
<td>Vascular</td>
<td>Includes focal neurological signs and symptoms</td>
<td>Control of cardiac and vascular risk factors</td>
</tr>
<tr>
<td>dementia</td>
<td>Radiologic evidence of stroke</td>
<td>Cls and memantine not effective</td>
</tr>
<tr>
<td></td>
<td>Onset within 3–6 mo of stroke</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Abrupt deterioration followed by stepwise progression</td>
<td></td>
</tr>
<tr>
<td>Lewy body dementia</td>
<td>Fluctuating cognition with pronounced variation in attention and alertness</td>
<td>Especially avoid typical antipsychotics, which may worsen motor symptoms</td>
</tr>
<tr>
<td></td>
<td>Recurrent visual hallucinations</td>
<td>May use Cls</td>
</tr>
<tr>
<td></td>
<td>Motor features of PD</td>
<td></td>
</tr>
<tr>
<td>Dementia of advanced PD</td>
<td>PD onset predates cognitive impairment</td>
<td>Especially avoid typical antipsychotics, which may worsen motor symptoms</td>
</tr>
<tr>
<td></td>
<td>Usually at latter stages of PD</td>
<td>May use Cls</td>
</tr>
<tr>
<td>Frontotemporal</td>
<td>Affects personality, behavior, self-care, and language</td>
<td>CIs may worsen behavior and cause agitation</td>
</tr>
<tr>
<td>dementia</td>
<td>Onset in ages 45–65 with a 2- to 10-yr course</td>
<td>SSRI or trazodone may be beneficial</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Reversible Causes</strong></td>
<td></td>
</tr>
<tr>
<td>Vitamin B\textsubscript{12} deficiency</td>
<td>Progressive memory loss</td>
<td>Replace vitamin B\textsubscript{12} according to standard protocols</td>
</tr>
<tr>
<td></td>
<td>Vitamin B\textsubscript{12} serum concentration &lt; 300 pg/mL</td>
<td></td>
</tr>
<tr>
<td></td>
<td>May be anemic also, but folic acid may disguise the anemia</td>
<td></td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>Deficient or inadequate replacement of thyroxine</td>
<td>Levothyroxine replacement according to standard protocols</td>
</tr>
<tr>
<td>Depression</td>
<td>Trouble concentrating and memory</td>
<td>Treatment of depression according to standard protocols</td>
</tr>
<tr>
<td></td>
<td>Apathy and “I don’t care” responses</td>
<td></td>
</tr>
<tr>
<td>NPH</td>
<td>Triad of progressive memory loss, incontinence, and gait abnormality</td>
<td>Surgical placement of ventricular shunt</td>
</tr>
<tr>
<td></td>
<td>Symptoms improve after lumbar puncture</td>
<td></td>
</tr>
</tbody>
</table>

AD = Alzheimer disease; CI = cholinesterase inhibitor; MCI = mild cognitive impairment; NPH = normal pressure hydrocephalus; PD = Parkinson disease; SSRI = selective serotonin reuptake inhibitor.

C. Assessment Tools

1. Folstein MMSE
   a. 30-point scale; higher is better function
   b. Untreated AD: Score usually decreases 3 or 4 points a year.
   c. Heavily relies on verbal and language skills, so less accurate if education is poor

2. SLUMS examination
   a. 30-point scale; higher number is better function
   b. Includes adjustment of scores for lower educational status
3. Montreal Cognitive Assessment
   a. 30-point scale; higher number is better function
   b. Less reliant on verbal or language skills
4. Mini-Cog assessment
   a. 5-point scale; higher number is better function
   b. Easiest to administer; takes 3 minutes

D. New Diagnostic Guidelines
1. Recognizes three phases
   a. Preclinical, asymptomatic phase
   b. Symptomatic, predementia phase (MCI)
   c. Dementia phase
2. Diagnosis may be identified for research purposes by:
   a. Biomarkers of increased tau or decreased β-amyloid concentrations in cerebrospinal fluid
   b. Reduced glucose uptake in brain on positron emission tomography scanning using florbetapir F 18 or flutemetamol F 18
   c. Atrophy of specific brain areas on magnetic resonance imaging
3. Preclinical and predementia phases are targets for investigational studies to halt progression.
4. For clinicians, diagnosis is given without these biomarkers or imaging.

E. Clinical Presentation and Classification

Table 4. Stages of AD

<table>
<thead>
<tr>
<th>Stages</th>
<th>MMSE (out of 30)</th>
<th>Examples of Cognitive Loss</th>
<th>Examples of Functional Loss</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>20–24</td>
<td>Some short-term memory loss; word-finding problems</td>
<td>Loss of IADLs such as laundry, housekeeping, and managing medications; may get lost in familiar places</td>
</tr>
<tr>
<td>Moderate</td>
<td>10–19</td>
<td>Disorientation to time and place, inability to engage in activities and conversation</td>
<td>Needs assistance with ADLs such as bathing, dressing, and toileting</td>
</tr>
<tr>
<td>Severe</td>
<td>&lt; 10</td>
<td>Loss of speech and ambulation, incontinence of bowel and bladder</td>
<td>Dependency in basic ADLs such as feeding oneself; often needs around-the-clock care</td>
</tr>
</tbody>
</table>

ADLs = activities of daily living; IADLs = instrumental activities of daily living; MMSE = Mini–Mental State Examination.

F. Management
1. Goals are to maintain function and cognition.
   a. Functional management and safety issues
   b. Legal considerations
2. Nonpharmacologic therapy
   a. Education, especially with caregiver
   b. Physical exercise and mental exercise
   c. Management of comorbid conditions
   d. Avoid alcohol and medications that worsen mentation.
3. Medical food: Caprylidene triglyceride
   a. Mechanism is to provide ketone bodies for the brain to use as an energy source when glucose metabolism is impaired.
   b. Not routinely used because study measures became nonsignificant
Patient Case

8. An 84-year-old widow lives at home alone. She can perform ADLs and most IADLs with her daughter’s assistance. Her current medications are hydrochlorothiazide 12.5 mg daily for hypertension, tolterodine long acting 4 mg daily for incontinence, escitalopram 20 mg daily for depression, acetaminophen 650 mg as needed for arthritis, and calcium/vitamin D for prevention of osteoporosis. The patient’s physician administers the MMSE, and her score is 23/30. On physical examination, no cogwheel rigidity or tremor is noted. Which recommendation would be best at this time?

A. Add donepezil 5 mg daily.
B. Discontinue tolterodine and reassess the patient.
C. Add vitamin B₁₂ 1000-mg injection monthly.
D. Change hydrochlorothiazide to lisinopril 5 mg daily.

4. Pharmacologic therapy

Table 5. Comparison of Drugs for AD Treatment

<table>
<thead>
<tr>
<th>Drug</th>
<th>Starting Dose</th>
<th>Maintenance Dose</th>
<th>Dosage Forms</th>
<th>Pharmacologic Properties</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cholinesterase Inhibitors</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Donepezil</td>
<td>5 mg daily</td>
<td>10 mg daily</td>
<td>Tablets</td>
<td>Acetylcholinesterase inhibitor; metabolized in part by CYP2D6 and CYP3A4</td>
<td>Labeled for mild to moderate and moderate to severe AD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>May increase to 23 mg/day</td>
<td>Orally disintegrating tablets</td>
<td>Protein binding 96%</td>
<td></td>
</tr>
<tr>
<td>Rivastigmine</td>
<td>1.5 mg twice daily</td>
<td>3–6 mg twice daily</td>
<td>Capsules</td>
<td>Acetyl- and butyryl-cholinesterase inhibitor</td>
<td>Labeled for mild to moderate and severe AD as well as mild to moderate dementia with Parkinson disease</td>
</tr>
<tr>
<td></td>
<td>4.6-mg patch daily</td>
<td>9.5-mg patch daily</td>
<td>Oral solution</td>
<td>Nausea, vomiting, and diarrhea seem more intense than with other CIs</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>may increase to 13.3-mg patch daily</td>
<td>Transdermal patch</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Galantamine</td>
<td>4 mg twice daily</td>
<td>8–12 mg twice daily</td>
<td>Tablets</td>
<td>Selective competitive, reversible acetylcholinesterase inhibitor and nicotine receptor modulator</td>
<td>Preferable to administer with food</td>
</tr>
<tr>
<td></td>
<td></td>
<td>8–24 mg ER once daily</td>
<td>Oral solution</td>
<td>Metabolized in part by CYP2D6 and CYP3A4</td>
<td>Renal dosing adjustment necessary</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>ER capsules</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glutamatergic Therapy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Memantine</td>
<td>5 mg once daily</td>
<td>10 mg twice daily</td>
<td>Tablets</td>
<td>N-methyl-D-aspartate receptor antagonist that blocks glutamate transmission</td>
<td>Labeled for moderate to severe AD; may be used in combination with acetylcholinesterase inhibitors</td>
</tr>
<tr>
<td></td>
<td>7 mg ER once daily</td>
<td>28 mg ER once daily</td>
<td>Oral solution</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>ER capsules</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Combination Product</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Donepezil/</td>
<td>10/28 mg once daily in the evening</td>
<td>10/28 mg once daily</td>
<td>ER capsule</td>
<td>Acetylcholinesterase inhibitor and N-methyl-D-aspartate receptor antagonist</td>
<td>Use after stabilized on donepezil and memantine separately</td>
</tr>
<tr>
<td>memantine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Renal dosing adjustment necessary</td>
</tr>
</tbody>
</table>

ER = extended release.
a. Adverse effects of CIs
   i. GI: Nausea, vomiting, diarrhea, elevated risk of GI bleeding
   ii. CNS: Headache, insomnia, dizziness
   iii. Cardiac: Bradycardia, orthostatic hypotension, syncope (AGS Beers Criteria note CIs as inappropriate drugs in patients with syncope)
   iv. Genitourinary: Incontinence
   v. Long-term adverse effects: Anorexia, weight loss, falls, hip fracture, pacemaker placement
b. Adverse effects of memantine: Agitation, urinary incontinence (UI), insomnia, diarrhea, dizziness, confusion, headache

   a. Initiate a CI in patients with mild to moderate AD.
   b. No evidence one agent is superior to others
   c. Titrate to recommended maintenance dose as tolerated.
   d. May increase to maximum dose if tolerated and maintenance dose no longer effective, but clinically meaningful improvement unlikely
   e. In moderate to severe disease, may use a CI, memantine, or both a CI and memantine
   f. Slight or no benefit with combination therapy in systematic reviews
   g. Studies find no benefit of memantine in mild AD.

6. Controversy over clinical significance of responses

Table 6. Evidence for Response to Drugs for AD

<table>
<thead>
<tr>
<th>Drug</th>
<th>Test</th>
<th>Testing Range</th>
<th>Response Difference Compared with Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>CI</td>
<td>AD Assessment Scale–Cognitive</td>
<td>0–70</td>
<td>–2.7</td>
</tr>
<tr>
<td>Memantine</td>
<td>Severe Impairment Battery</td>
<td>0–100</td>
<td>2.97</td>
</tr>
</tbody>
</table>

7. Therapy duration
   a. In general, need 3–6 months to evaluate for objective benefit with tools
   b. Longest study was for 52 weeks, but many receive the drug for years.
   c. The Choosing Wisely criteria recommend evaluating at 12 weeks and considering discontinuation if the goals of therapy are not met.
   d. In general, discontinue at advanced stages of disease. Tapering is recommended if the patient is taking a high dose.
   e. Some rebound agitation may occur.

8. Herbals and dietary supplements
   a. Vitamin E was not shown effective in most large prospective trials. A recent randomized controlled trial of 613 veterans with mild to moderate AD using 2000 international units/day over 2 years showed a delay in clinical progression of 19% per year.
   b. Gingko biloba was not effective in prevention or treatment in randomized controlled trials.
   c. Observational studies support the effect of the Mediterranean diet, exercise, and curcumin (turmeric).
Patient Cases

9. An 87-year-old man with AD receives rivastigmine 6 mg twice daily. His family notes improved functional ability but reports that he has nausea and vomiting that appear to be related to rivastigmine. Which recommendation is best for the patient at this time?
   A. Advise the patient to take rivastigmine with an antacid.
   B. Change rivastigmine to the patch that delivers 9.5 mg daily.
   C. Discontinue rivastigmine and initiate memantine 5 mg twice daily.
   D. Add prochlorperazine 25 mg by rectal suppository with each rivastigmine dose.

10. A 75-year-old woman with AD who lives at home with her husband has been treated with donepezil 10 mg daily for about 3 years. When she began therapy, her MMSE score was 21/30; her present MMSE score is 17/30. The patient cannot perform most IADLs but can perform most ADLs with cueing. About 2 months ago, her donepezil dose was increased to 23 mg, but she could not tolerate it, and it was reduced back to 10 mg daily. Her husband asks about changing her drug treatment to help maintain her function. Which is the next best course of action?
   A. Retry donepezil 23 mg daily.
   B. Initiate memantine 5 mg daily.
   C. Add vitamin E 400 units twice daily.
   D. Change donepezil to rivastigmine 9.5-mg patch daily.

III. BEHAVIORAL AND PSYCHOLOGICAL SYMPTOMS OF DEMENTIA

A. Epidemiology
   1. As disease progresses from mild to moderate, behavioral and psychological symptoms of dementia (BPSD) occur. These tend to wane as the disease progresses to severe.
   2. Up to 90% of patients with dementia have BPSD at some point in disease progression.
   3. Associated with high rate of disability, functional decline, poor health outcomes, physical injury, nursing home placement, and emergency services.
   4. Behaviors commonly peak during late afternoon or early evening and are thus called “sundowning.”

Table 7. Symptoms During Disease Progression

<table>
<thead>
<tr>
<th>MMSE Score</th>
<th>Stage</th>
<th>Symptoms</th>
<th>Noncognitive Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>25</td>
<td>Mild</td>
<td>• Memory loss</td>
<td>• Mood swings(^a)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Apathy</td>
<td>• Mild executive function</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Poor drawing</td>
<td>• Mild personality changes(^a)</td>
</tr>
<tr>
<td>20</td>
<td>Moderate</td>
<td>• Unable to learn</td>
<td>• Aggression, psychosis(^a)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Aphasia, apraxia</td>
<td>• Confusion, insomnia(^a)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Wandering, agitation(^a)</td>
<td>• Need ADL assistance</td>
</tr>
<tr>
<td>15</td>
<td>Severe</td>
<td>• Gait changes(^a)</td>
<td>• Loss of ADLs</td>
</tr>
<tr>
<td>10</td>
<td></td>
<td>• Incontinence</td>
<td>• Confined to bed</td>
</tr>
<tr>
<td>5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\(^a\)Noncognitive symptoms.
B. Assessment
1. Scales are rarely used in nursing home or clinical practice, but it is important to identify the target behavior, how often it is occurring, and how severe it is in order to assess the treatment response.
2. Assess for a medical reason that may precipitate the target behavior and treat it, if found.
   a. Pain is a common issue that patients cannot communicate. Treat with scheduled acetaminophen.
   b. Delirium precipitated by medical illness or medication should be ruled out.

C. Nonpharmacologic Treatment: Cornerstone of Therapy
1. The theory is that behavior is the communication of unmet need.
2. Eliminate antecedents and triggers.
3. Person-centered interventions: Consider long-standing habits, values, and beliefs of patient; use distraction, music, aromatherapy, and pet therapy.
4. Symptoms likely to respond: Wandering, hoarding, hiding objects, repetitive questioning, withdrawal, social inappropriateness, apathy

D. Pharmacologic Treatment: None of these are U.S. Food and Drug Administration (FDA)-labeled indications.
1. Agency for Healthcare Research and Quality has published a summary on the use of atypical antipsychotic agents for off-label indications. Atypical antipsychotics improve behavioral symptoms of dementia, but effect sizes are small (number needed to treat 5–14), and adverse effects are significant (number needed to harm [NNH] 100).
2. Retrospective case-control study of older veterans with dementia during a 180-day period indicates haloperidol NNH = 8, compared with atypical antipsychotics with NNH = 14–31 for risk of death

Table 8. Drug Treatment for BPSD

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Presentation</th>
<th>Treatment Options After Nonpharmacologic Efforts Ineffective</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anxiety</td>
<td>Part of this is because they cannot remember things</td>
<td>Buspironone or SSRI/SNRI or gabapentin Limit benzodiazepines</td>
</tr>
<tr>
<td>Apathy</td>
<td>One of the earliest symptoms Nonpharmacologic treatment tailored to patient’s activities</td>
<td>CIs Methylphenidate effective in small, short-term studies</td>
</tr>
<tr>
<td>Depression</td>
<td>Up to 80% of patients with AD have depression</td>
<td>SSRI or mirtazapine</td>
</tr>
<tr>
<td>Insomnia</td>
<td>Sleep-wake cycle is disrupted</td>
<td>Melatonin</td>
</tr>
<tr>
<td>Wandering</td>
<td>Walk so much they begin to lose weight</td>
<td>No drug will stop patients from wandering</td>
</tr>
<tr>
<td>Paranoia, halluci-</td>
<td>They may think because they cannot find something, you stole it Often accuse spouse of infidelity</td>
<td>Risperidone, olanzapine, quetiapine, or aripiprazole has been tried. Use very low doses. ADEs may offset any benefit</td>
</tr>
<tr>
<td>sundowning</td>
<td>If psychosis and delusions do not bother anyone, do not use drugs</td>
<td></td>
</tr>
<tr>
<td>Aggression, resistance to care</td>
<td>Most difficult and best response is to treat nonpharmacologically</td>
<td>Drugs under investigation for agitation include prazosin, dextromethorphan/quinidine, and citalopram</td>
</tr>
</tbody>
</table>

ADE = adverse drug effect; BPSD = behavioral and psychological symptoms of dementia; SNRI = serotonin-norepinephrine reuptake inhibitor.
Patient Case
Questions 11 and 12 pertain to the following case.

11. You are evaluating the medication profile of an 87-year-old woman who resides in a secure advanced dementia unit. Her medical history includes dementia (likely AD), Parkinson disease, and OA. She needs assistance with all ADLs, including total assistance with bathing and dressing, as well as help with feeding. She transfers with minimal help to a wheelchair. Her medication regimen includes donepezil 10 mg daily, memantine 10 mg twice daily, carbidopa/levodopa 25/100 mg four times daily, and a multivitamin supplement daily. The patient’s most recent MMSE score is 5/30. When reviewing the nursing notes, you see several references to the patient’s continually crying out, “Help me, help me,” beginning around 5 p.m. On medical evaluation, reversible causes of her hypervocalization are ruled out. Which initial approach is most appropriate for this patient?
   A. Initiate ibuprofen 400 mg every 8 hours.
   B. Order haloperidol 1 mg every 6 hours as needed for agitation.
   C. Begin music therapy with songs the patient enjoyed when younger.
   D. Move the patient to a private room to minimize social contacts after 3 p.m.

12. After 2 months, the patient’s agitation increases such that the nursing staff cannot bathe or feed her. Assuming nonpharmacologic approaches are ineffective, which is the best pharmacologic approach to treat her behavioral symptoms?
   A. Increase donepezil to 23 mg daily.
   B. Begin melatonin 6 mg at bedtime.
   C. Add quetiapine 25 mg at 4 p.m. daily.
   D. Add citalopram 10 mg daily.

IV. URINARY INCONTINENCE

A. Epidemiology
   1. Prevalence in community-dwelling older adult women is 38%.
   2. Less common in older adult men: 17%.
   3. Up to 75% of nursing home residents have UI.
   4. Transient incontinence can occur because of DRIP:
      D = Drugs, Delirium
      R = Retention, Restricted Mobility
      I = Impaction, Infection, Inflammation
      P = Polyuria, Prostatitis

B. Physiology
   1. During filling, β3-adrenergic stimulation relaxes detrusor to increase capacity.
   2. α-Adrenergic stimulation tightens the internal bladder sphincter.
   3. Acetylcholine (M3 receptors) mediates involuntary and volitional bladder contractions.
   4. Normal bladder emptying occurs with a decrease in urethral resistance and contraction of the bladder muscle.
   5. Aging effects include decreased bladder elasticity and capacity, more frequent voiding, decline in bladder outlet and urethral resistance in women with loss of estrogen, and decrease in flow rate in men with prostatic enlargement.
C. Types of UI

Table 9. Common Types of UI and Drug-Induced Causes

<table>
<thead>
<tr>
<th>Type of Incontinence</th>
<th>Description</th>
<th>Drug-Induced Causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urge or overactive bladder</td>
<td>Loss of a moderate amount of urine with an increased need to void. Detrusor instability can be caused by CNS damage from a stroke.</td>
<td>Cholinergic agents that stimulate the bladder such as bethanechol and CIs.</td>
</tr>
<tr>
<td>Stress incontinence</td>
<td>Loss of small amounts of urine with increased abdominal pressure (e.g., sneezing, coughing). Stress UI is more common in postmenopausal women.</td>
<td>α-Blockers such as prazosin decrease urethral sphincter tone.</td>
</tr>
<tr>
<td>Overflow incontinence</td>
<td>Loss of urine because of excessive bladder volume caused by outlet obstruction or an acontractile detrusor. PVR is often high (&gt; 300 mL), indicating incomplete emptying.</td>
<td>Anticholinergic agents, calcium channel blockers, and opioids decrease detrusor muscle contractions.</td>
</tr>
<tr>
<td>Functional incontinence</td>
<td>Inability to reach the toilet because of mobility constraints.</td>
<td>Sedating drugs that cause confusion. Diuretics increase voiding.</td>
</tr>
<tr>
<td>Mixed incontinence</td>
<td>UI that has more than one cause, usually stress and overactive bladder.</td>
<td></td>
</tr>
</tbody>
</table>

PVR = postvoid residual; UI = urinary incontinence.

D. Nonpharmacologic Interventions

1. Exercise and weight loss for patients with a body mass index greater than 25–30 kg/m²
2. Stress
   a. Pelvic floor exercises (Kegel exercises) are first line for stress.
   b. Biofeedback may be needed to teach pelvic floor exercises.
   c. Stress incontinence usually responds to surgical repair.
   d. Pessaries or bulking agent injections also help stress incontinence.
3. Urge
   a. Pelvic floor exercises in combination with medication for urge or mixed UI.
   b. Bladder training to increase time between voiding in urge incontinence.
   c. Peripheral tibial nerve stimulation or sacral neuromodulation techniques are third line after lifestyle and pharmacologic treatments.
4. Scheduled and timed voiding may be helpful for patients with dementia.
5. Prostatectomy in men or self-catheterization for severe overflow incontinence.
### E. Drug Treatment

#### Table 10. Recommended Drug Treatment by Type of Incontinence

<table>
<thead>
<tr>
<th>Type of Incontinence</th>
<th>Drug Treatment</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urge or overactive bladder</td>
<td>Antimuscarinic and anticholinergic agents&lt;br&gt;Oxybutynin, tolterodine, fesoterodine, trospium, solifenacin, darifenacin</td>
<td>Magnitude of clinical efficacy is modest&lt;br&gt;Differences in adverse reactions exist, but clinical differences in efficacy between these agents have not been shown&lt;br&gt;Longer-acting formulations may be better tolerated</td>
</tr>
<tr>
<td>β3-Agonist</td>
<td>Mirabegron</td>
<td>Appears well tolerated but has not been compared with antimuscarinics</td>
</tr>
<tr>
<td>OnabotulinumtoxinA</td>
<td>Intradetrusor or injections</td>
<td>Prevents stimulation of detrusor muscle&lt;br&gt;Pre-procedure antibiotic recommended&lt;br&gt;May cause urinary retention; must be able to perform self-catheterization</td>
</tr>
<tr>
<td>Stress</td>
<td>α-Adrenergic agonists&lt;br&gt;Pseudoephedrine, phenylephrine</td>
<td>Efficacy evidence is limited</td>
</tr>
<tr>
<td>Topical estrogens</td>
<td>Conjugated estrogen vaginal cream or estradiol vaginal insert or ring</td>
<td>Use if other symptoms of estrogen deficiency&lt;br&gt;Vaginal estrogens may improve severity of stress incontinence</td>
</tr>
<tr>
<td>Serotonin/norepinephrine reuptake inhibitor</td>
<td>Duloxetine</td>
<td>Not FDA labeled for stress UI; may reduce the severity of incontinence&lt;br&gt;Not significantly different from placebo for symptoms&lt;br&gt;Adverse effects may limit its usefulness</td>
</tr>
<tr>
<td>Overflow</td>
<td>α-Adrenergic antagonists&lt;br&gt;Alfuzosin, tamsulosin, silodosin, doxazosin, terazosin, prazosin</td>
<td>Adverse effects vary depending on selectivity to receptors in the bladder or prostate (alfuzosin, silodosin, and tamsulosin are more specific and preferred in older adults)</td>
</tr>
<tr>
<td>5-α-reductase inhibitors</td>
<td>Finasteride, dutasteride</td>
<td>To slow progression&lt;br&gt;Reduce the size of the prostate and alter PSA values</td>
</tr>
<tr>
<td>Cholinomimetics</td>
<td>Bethanechol</td>
<td>Stimulates the detrusor muscle but also systemic cholinomimetic effects</td>
</tr>
<tr>
<td>Phosphodiesterase type 5 inhibitors</td>
<td>Tadalafil</td>
<td>5 mg once daily approved for BPH</td>
</tr>
<tr>
<td>Functional</td>
<td>No drug treatments</td>
<td>Consider interventions to remove any potential cause, barriers, or obstacles; provide schedules or prompted toileting; assistance may be required to transfer on and off commode</td>
</tr>
<tr>
<td>Mixed</td>
<td>Focus on predominating symptoms</td>
<td>Consider treatments for individual components (i.e., stress and urge)</td>
</tr>
</tbody>
</table>

BPH = benign prostatic hypertrophy; PSA = prostate-specific antigen.
Table 11. Comparison of Adverse Effects from Urinary Antimuscarinic Agents

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dry Mouth</th>
<th>Constipation</th>
<th>Dizziness/Fatigue</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxybutynin</td>
<td>71.4%</td>
<td>15.1%</td>
<td>16.6%</td>
</tr>
<tr>
<td>Oxybutynin ER/XL</td>
<td>up to 72%</td>
<td>up to 15%</td>
<td>≥ 5%</td>
</tr>
<tr>
<td>Oxybutynin TDS</td>
<td>4.1%–9.6%</td>
<td>3.3%</td>
<td>N/A</td>
</tr>
<tr>
<td>Oxybutynin gel</td>
<td>12.1%</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Tolterodine IR, ER</td>
<td>23%–35%</td>
<td>6%–7%</td>
<td>2%–5%</td>
</tr>
<tr>
<td>Fesoterodine</td>
<td>18.8%–34.6%</td>
<td>4.2%–6%</td>
<td>&lt; 1%</td>
</tr>
<tr>
<td>Trosplum</td>
<td>20.1%</td>
<td>9.6%</td>
<td>1.9%</td>
</tr>
<tr>
<td>Solifenacin</td>
<td>10.9%–27.6%</td>
<td>5.4%–13.4%</td>
<td>1%–2.1%</td>
</tr>
<tr>
<td>Darifenacin</td>
<td>20.2%–35.3%</td>
<td>14.8%–21.3%</td>
<td>0.9%–2.1%</td>
</tr>
<tr>
<td>Mirabegron</td>
<td>N/A</td>
<td>1.6%</td>
<td>1.2%–1.4%</td>
</tr>
</tbody>
</table>


ER/XL = extended release; IR = immediate release; TDS = transdermal delivery system.

Patient Case

13. A 75-year-old woman reports urinary urgency, frequency, and loss of urine when she cannot get to the bathroom in time. She also wears a pad at night that she changes two or three times because of incontinence. Her medical history is significant for MCI (MMSE score 25/30), OA, and hypothyroidism. A urinalysis is negative. Physical examination is normal, and her PVR is normal (less than 100 mL). Which therapy would be best to initiate for this patient at this time?
   A. Mirabegron.
   B. Darifenacin.
   C. Pelvic floor exercises and solifenacin.
   D. Pelvic floor exercises and tolterodine immediate release.

V. BENIGN PROSTATIC HYPERTROPHY

A. Epidemiology
   1. BPH usually develops after age 40.
   2. By age 60, 50% of all men have BPH; by age 85, 90% have BPH.

B. Pathophysiology and Clinical Presentation
   1. Type II 5-α-reductase facilitates conversion of testosterone to dihydrotestosterone, resulting in prostate growth.
   2. Lower urinary tract symptoms (LUTS) occur in 25% of men.
      a. Voiding (obstructive) symptoms: Decreased force, hesitancy, dribbling
      b. Storage (irritative) symptoms: Urinary urgency, frequency, nocturia, dysuria
   3. The American Urological Association Symptom Index (AUASI) score can help determine severity and appropriate treatment. The index consists of seven questions evaluating the severity of LUTS on a 0–5 scale. Higher numbers indicate more severe symptoms.
C. Evaluation
1. Medical history, digital rectal examination, BUN, SCr, and urinalysis
2. If prostate cancer is suspected, plan treatment with a 5-α-reductase inhibitor, prostate-specific antigen (PSA)
3. If significant urinary retention is suspected, need to assess PVR. If PVR is greater than 50 mL, patients have an elevated risk of infection.
4. Assess for medications that may exacerbate BPH symptoms.
   a. α-Adrenergic agonists (decongestants) can stimulate smooth muscle contraction in the prostate and urethra, obstructing urinary flow through the urethra.
   b. Anticholinergic drugs (urinary and GI antispasmodics, antihistamines, tricyclic antidepressants, phe-nothiazines) can reduce the ability of the bladder detrusor muscle to contract and empty the bladder.
   c. Diuretics can increase urinary frequency and volume.
   d. Testosterone replacement can stimulate prostate growth.
5. If the AUASI score is 0–7 (mild), use watchful waiting.
6. Patients with high AUASI scores of 20 and more (severe disease) should be assessed for prostatectomy.
7. Patients with moderate disease (scores 8–19) are candidates for medical treatment.

D. Drug Treatment
1. α-Adrenergic blockers: These relieve LUTS in men with moderate or severe AUASI scores by reducing smooth muscle contractions in the urethra and surrounding tissues.
   a. Nonspecific α-adrenergic blockers such as doxazosin and terazosin also lower blood pressure significantly.
   b. Newer agents are uroselective antagonists of α₁-adrenergic receptors (tamsulosin, silodosin) and selective antagonists of postsynaptic α₁-adrenergic receptors (alfuzosin) in the prostate and bladder. They may have less associated hypotension.
   c. All α-blockers can cause hypotension.
   d. Compared with placebo, α-blockers lower the AUASI score by 4–6 points in patients with LUTS and BPH.
   e. All α-blockers are metabolized through the CYP3A4 pathway and have drug interactions with strong CYP3A4 inhibitors and inducers.
   f. Intraoperative floppy iris syndrome is a concern with α-blockers, especially tamsulosin. Men with LUTS being offered α-blockers should be asked about planned cataract surgery. Men with planned cataract surgery should avoid starting α-blockers until their cataract surgery is completed. If already taking an α-blocker, the patient needs to inform his surgeon so that precautions can be taken.
2. α-Reductase inhibitors
   a. These agents prevent the conversion of testosterone to dihydrotestosterone, modify the disease course, and may reduce the risk of urinary retention and surgical interventions.
      i. Finasteride competitively inhibits type II 5-α-reductase and lowers prostatic dihydrotestosterone by 80%–90%.
      ii. Dutasteride is a nonselective inhibitor of both type I and II 5-α-reductase. Prostatic dihydrotestosterone production is quickly suppressed with this agent.
      iii. Despite these pharmacologic differences, finasteride and dutasteride did not differ in trials; both reduce prostate size.
   b. α-Reductase inhibitors do not immediately reduce LUTS and should be reserved for use in men with large prostate volume (more than 40 g). At least 6 months of therapy is usually needed for clinical benefit. Prostate size may be reduced by about 25% during this interval.
   c. PSA concentrations are used to monitor for prostate cancer. Because these agents lower PSA concentrations, a baseline PSA test is recommended before initiating α-reductase inhibitors.
   d. Long-term therapy with an α-reductase inhibitor can increase the risk of high-grade tumors of the prostate in healthy men without a history of prostate cancer.
3. Phosphodiesterase type 5 inhibitors
   a. Tadalafil 5 mg once daily is approved for use in BPH.
   b. Mechanism is thought to be caused by phosphodiesterase-induced smooth muscle relaxation in the bladder, urethra, and prostate.
   c. Studied as monotherapy; the FDA does not recommend use in combination with α-blockers because the combination has not been adequately studied for BPH, and there is a risk of lowering the blood pressure. May be used in practice to treat both BPH and erectile dysfunction with a 4-hour separation of doses

4. Combination therapy
   a. May be needed in men with LUTS, a larger prostate size, and an elevated PSA
   b. Finasteride and doxazosin are the best studied; dutasteride is FDA label approved for use with tamsulosin in symptomatic men having an enlarged prostate.
   c. Two large clinical trials (Medical Therapy of Prostatic Symptoms [MTOPS] and the Combination of Avodart and Tamsulosin studies [CombAT]) evaluated monotherapy compared with combination therapy and concluded that in men with LUTS and an enlarged prostate, further benefit can be achieved using the two drugs in combination.

5. Supplements
   a. Saw palmetto plant extract (Serenoa repens)
      i. Conflicting evidence about the efficacy of saw palmetto in relieving LUTS; 2012 systematic review suggested no benefit over placebo
      ii. Using this agent with 5-α-reductase inhibitors may reduce the efficacy of the reductase inhibitors.
   b. β-Sitosterol, Pygeum africanum show some benefit, but short-term studies

6. Surgery is preferred in men with severe symptoms and in those with moderate symptoms who have not adequately responded to medical options.

7. Anticholinergic agents can be appropriate and effective alternatives in men without an elevated PVR when LUTS are predominantly storage (irritative) symptoms.

Table 12. Comparison of Drugs for BPH

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dose Range</th>
<th>Select Adverse Effects</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Terazosin</td>
<td>1–10 mg daily</td>
<td>Orthostatic hypotension</td>
<td>Initiate at low dose; can titrate every 2–7 days Start at bedtime</td>
</tr>
<tr>
<td>Doxazosin</td>
<td>1–8 mg daily</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alfuzosin ER</td>
<td>10 mg daily</td>
<td>Orthostatic hypotension</td>
<td>No need to titrate Take after a meal</td>
</tr>
<tr>
<td>Tamsulosin modified release</td>
<td>0.4–0.8 mg daily</td>
<td>May cause less orthostasis Causes ejaculatory dysfunction</td>
<td>Start at bedtime</td>
</tr>
<tr>
<td>Silodosin</td>
<td>8 mg daily</td>
<td>Causes ejaculatory dysfunction; appears less sedating</td>
<td>Contraindicated if CrCl &lt; 30 mL/min/1.73 m² Take with food</td>
</tr>
<tr>
<td></td>
<td>4 mg daily if CrCl 30–50 mL/min/1.73 m²</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Finasteride</td>
<td>5 mg daily</td>
<td>Decreased libido</td>
<td>Onset of action is usually 6 mo Monitor PSA Pregnancy category X</td>
</tr>
<tr>
<td>Dutasteride</td>
<td>0.5 mg daily 0.5/0.4 mg daily</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dutasteride/tamsulosin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tadalafil</td>
<td>5 mg daily</td>
<td>Orthostatic hypotension</td>
<td>Avoid use with α-blockers No data in combination or with long-term use</td>
</tr>
</tbody>
</table>
**Patient Case**

14. An 85-year-old man with LUTS visits his physician, who determines his AUASI score is 15. His blood pressure is 118/70 mm Hg sitting. A digital rectal examination confirms the diagnosis of BPH, and the physician schedules a further workup including a prostate ultrasound, which shows a prostate volume of 31 g. Which therapy is best at this time?

A. Terazosin.
B. Finasteride plus saw palmetto.
C. Tamsulosin.
D. Finasteride plus tamsulosin.

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### VI. OSTEOARTHRITIS

A. Epidemiology

1. OA is the most prevalent form of arthritis, affecting more than 46 million Americans.
2. Highly associated with aging: Large weight-bearing joints (e.g., hip and knee) are commonly affected.

B. Etiology and Pathophysiology

1. Risk factors include age, female sex, obesity, genetics, sports activities, occupation, previous injury, acromegaly, and other chronic illnesses.
2. Loss of cartilage occurs in the joint as the balance of chondrocyte function shifts from formation to destruction. Secondary inflammation and production of cytokines play a role.
3. Subchondral bone and the synovium are damaged, and the joint space narrows.
4. Single injuries or repeated micro-injuries may initiate or accelerate process.
5. Symptoms of pain result from activation of nociceptive nerve endings in the damaged joint.
6. Therapy goals: Relieve pain and swelling, maintain or improve joint function, prevent loss of function, and maintain or improve quality of life.

C. Nonpharmacologic Treatment

1. Patient education: Lifestyle, expectations, when to seek care
2. Weight loss decreases the biomechanical load on large weight-bearing joints; even a small amount of weight loss helps decrease pain and disability.
3. Exercise
4. Physical and occupational therapy
5. Surgery

D. Drug Therapy

1. Acetaminophen is first line, with as-needed doses followed by scheduled dosing to maximum of 3 g daily in divided doses (over-the-counter dose). Maximum of 4 g daily may be allowed for healthy older adults with closer monitoring by health care team.
   a. 1000 mg every 6 hours for up to three times daily or 650 mg every 6 hours
   b. Ensure that the patient knows to watch for “hidden” acetaminophen in other products.
   c. Monitor for hepatotoxicity in patients with an elevated risk of liver disease (previous liver problems, heavy alcohol consumption) with periodic liver function tests.
2. NSAIDs are used if acetaminophen response is inadequate in select patients.
   a. Avoid chronic use, or if necessary, use a cyclooxygenase-2 (COX-2) selective NSAID or add a pro-
      ton pump inhibitor to reduce the risk of GI bleeding. This recommendation is especially important
      for older adults.
   b. If one NSAID is not effective, change to others.
   c. Monitor for adverse effects: Rash, abdominal pain, GI bleeding, renal impairment, hypertension,
      heart failure, and drug-drug interactions
   d. Patients taking aspirin (for cardiac disease) should be educated to take aspirin at least 30 minutes
      before their first daily NSAID dose in the morning to avoid any interactions or reductions in aspirin
      efficacy. Naproxen appears to be safest with respect to cardiac risk.
   e. Monitor in chronic users: Complete blood cell count, BUN, SCr, and aspartate aminotransferase at
      least annually

3. Topical agents: Helpful for knees or smaller joints near surface of skin. Limited efficacy for widespread
   joint pain
   a. Capsaicin difficult to administer: Wear gloves, avoid contact with eyes, and do not skip doses.
      Local irritation occurs in 40% of patients.
   b. Diclofenac 1% gel (or patch is FDA labeled for minor trauma): Four short-term trials showed a 50%
      reduction in pain in 40% of subjects (number needed to treat = 5); longer-term trials had number
      needed to treat of 10. Comparative trials with oral administration showed no difference in the pro-
      portion of patients who received pain relief.

4. Intra-articular glucocorticoid injections
   a. Methylprednisolone or triamcinolone 10- to 40-mg injection depending on size of joint; may be
      repeated every 3 months
   b. Primary adverse effects are risk of septic arthritis, synovitis

5. Intra-articular hyaluronan may be used if glucocorticoid injections are ineffective.
   a. Meta-analysis indicates effects last up to 30 weeks.
   b. Frequency of injection undetermined: Annual or more often?

6. Alternative dietary supplements: Glucosamine sulfate, 400–500 mg taken three times daily, with or
   without chondroitin 400 mg, may be considered for chronic therapy to prevent joint degradation and
   relieve pain
   a. Evidence to support treatment is contradictory; many studies are low quality.
   b. The adverse effect profile of glucosamine/chondroitin is similar to that of placebo.

7. Opioids
   a. Patients with persistent, moderate to severe pain from OA who do not respond to more conservative
      strategies are candidates for opioids. AGS recommends opioids for OA rather than chronic use of
      NSAIDs when older patients do not respond to initial acetaminophen therapy.
   b. Hydrocodone/acetaminophen combination is now schedule II.
   c. Tramadol alone or in combination with acetaminophen is an alternative when NSAIDs are ineffective
      or contraindicated.
   d. Stronger opioids can be more effective but can incur more significant adverse effects.
   e. Monitor and anticipate opioid adverse effects, and treat accordingly.
Patient Case
15. An 85-year-old man presents with pain from hip OA. He has hypertension, coronary artery disease, and BPH. For his OA, he has been taking acetaminophen 650 mg three times daily. He reports that acetaminophen helps but that the pain persists and limits his ability to walk. Which is the best next step for this patient?
   A. Change acetaminophen to celecoxib.
   B. Add hydrocodone.
   C. Change acetaminophen to ibuprofen.
   D. Add glucosamine.

VII. RHEUMATOID ARTHRITIS

A. Epidemiology
   1. A systemic disease characterized by a bilateral inflammatory arthritis that usually affects the small joints of the hands, wrists, and feet
   2. The prevalence is estimated to be 1%–2%, with women predominating until after age 60, when prevalence becomes equal.
   3. RA can occur at any age but has an increasing prevalence up to age 70.
   4. RA is an autoimmune disease with a strong genetic predisposition.

B. Pathophysiology and Clinical Presentation
   1. Chronic inflammation of the synovium leads to proliferation and development of a pannus.
   2. The pannus invades joint cartilage and eventually causes erosion of the bone and joint destruction.
   3. The cause of the initial inflammatory activation is unknown, but once activated, the immune system produces antibodies and cytokines that accelerate cartilage and joint destruction.
   4. Patients present with joint pain and stiffness, fatigue, and other inflammatory symptoms. Symptoms also include warmth, redness, and swelling of the joints, usually with symmetrical distribution.
   5. Laboratory tests often show a positive rheumatoid factor (RF), elevated sedimentation rate, C-reactive protein, anti–cyclic citrullinated peptide antibodies, and normochromic normocytic anemia.
   6. RA can also affect other organs, causing pulmonary fibrosis, vasculitis, and dry eyes.

C. Treatment
   1. The treatment goal is to control the inflammatory process so that disease remission occurs. This leads to relief of pain, maintenance of function, and improved quality of life. Treatment response can be measured by:
      a. Reduction in the number of affected joints and in joint tenderness and swelling
      b. Improvement in pain
      c. Decreased amount of morning stiffness
      d. Reduction in serologic markers such as RF
      e. Improvement in quality-of-life scales
   2. Nonpharmacologic treatment: Concurrent with pharmacologic treatment
      a. Rest during periods of disease exacerbation
      b. Occupational and physical therapy to support mobility and maintain function
      c. Maintenance of a normal weight (avoid overweight and obesity) to reduce biomechanical stress on joints
      d. Assistive devices if needed
      e. Surgery for tendons or joints
3. Disease-modifying antirheumatic drugs (DMARDs)
   a. Initiate DMARD within 3 months of diagnosis (methotrexate preferred).
   b. Step-down approach: Start with DMARD (one or more, depending on disease severity) together with anti-inflammatory drug (NSAID, steroid). As pain is controlled, reduce anti-inflammatory agent. As joint damage and inflammation is controlled, reduce DMARD slowly. Do not discontinue all DMARDs, even if patient is in remission.
   c. Nonbiologic DMARDs are first line.
      i. Methotrexate has the most long-term data and better outcomes.
      ii. Hydroxychloroquine has slow onset of action.
      iii. Sulfasalazine is the drug of choice in pregnancy but also has slow onset.
      iv. Leflunomide substitutes, with efficacy comparable with methotrexate.
      v. Some patients with poor prognostic indicators such as functional limitation, extra-articular disease, positive RF, anti–cyclic citrullinated peptide antibodies, or bony erosions on radiography may be candidates for combination DMARD therapy.
   d. Biologic DMARDs are used in combination with methotrexate for severe disease or as alternatives if nonbiologic DMARDs are ineffective or contraindicated.
      i. Tumor necrosis factor (TNF) inhibitors: Etanercept, infliximab, adalimumab, certolizumab, golimumab
      ii. Non-TNF biologics: Abatacept, anakinra, rituximab, tocilizumab
      iii. Biologic kinase inhibitor: Tofacitinib
   e. Etanercept, infliximab, abatacept, or rituximab is most often used.

4. NSAIDs, glucocorticosteroids, or both can be used for immediate pain and inflammation relief.
   a. NSAIDs do not affect disease progression in RA; their anti-inflammatory effect occurs within 1–2 weeks of daily dosing, whereas the analgesic effect begins within several hours of administration.
   b. Glucocorticosteroids (dosed at 10 mg daily or less) are not recommended for long-term use because of their many adverse effects and long-term complications. They are often used as bridge therapy to provide anti-inflammatory effects while waiting for the DMARDs to take effect.

D. Comorbid Conditions
   1. Patients with RA are more likely to develop other chronic diseases either from the effects of RA or from the medications used to treat RA.
   2. Cardiovascular disease (myocarditis and heart failure) causes 40% of all deaths in patients with RA. Low-dose aspirin, omega-3 fatty acids, statins, or combination therapy should be considered.
      a. Follow standard guidelines to lower cardiovascular risk factors.
      b. European guidelines recommend multiplying risk score by 1.5 for patients with RA who have disease of 10 years or more, are positive for RF or anti–cyclic citrullinated peptide, or have severe extra-articular disease manifestations (two of the three should be present).
      c. In a patient with congestive heart failure, it is recommended to avoid TNF inhibitors.
   3. Infection risk is elevated, particularly pulmonary infections and sepsis. A history of tuberculosis or hepatitis B calls for extra vigilance.
      a. Tuberculosis screening is required for patients who are considered for therapy with biologic DMARDs.
      b. Immunizations are best given before initiating DMARDs or biologics. A 2-week waiting period is recommended.
      c. Avoid zoster or other live vaccines while the patient is taking DMARDs or biologics.
      d. Patients with hepatitis B or C, if treated with effective antivirals, are treated the same as patients without hepatitis; however, with untreated disease, DMARDs are preferred to TNF inhibitors.
Table 13. Selected DMARDs for RA

<table>
<thead>
<tr>
<th>Drug</th>
<th>Customary Dose</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Nonbiologic DMARDs</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Methotrexate</td>
<td>7.5–15 mg every week</td>
<td>First-line DMARD for RA; monitor for myelosuppression, liver dysfunction, and pulmonary fibrosis; a teratogen</td>
</tr>
<tr>
<td>Leflunomide (Arava)</td>
<td>10–20 mg/day</td>
<td>Similar to methotrexate; an initial loading dose may give therapeutic response within the first month</td>
</tr>
<tr>
<td>Hydroxychloroquine (Plaquenil)</td>
<td>200–300 mg twice daily</td>
<td>Must routinely monitor for ocular toxicity; however, this agent has a better adverse effect profile overall</td>
</tr>
<tr>
<td>Sulfasalazine</td>
<td>500–1000 mg twice daily</td>
<td>GI adverse effects often limit the use of this agent</td>
</tr>
<tr>
<td><strong>Biologic DMARDs</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>TNF Inhibitors</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Etanercept (Enbrel)</td>
<td>50 mg SC weekly</td>
<td>Binds to TNF, inactivating this cytokine; generally well tolerated; usually used in those whose methotrexate therapy fails; monitor for infection; check baseline PPD</td>
</tr>
<tr>
<td>Infliximab (Remicade, biosimilar version)</td>
<td>3 mg/kg IV at 0, 2, and 6 wk; then every 8 wk thereafter</td>
<td>A mouse/human chimeric antibody to TNF; used in combination with methotrexate to prevent formation of antibodies to this protein; monitor for infection; check baseline PPD</td>
</tr>
<tr>
<td>Adalimumab (Humira)</td>
<td>40 mg SC every 2 wk</td>
<td>Human antibody to TNF; less antigenic than other TNF antibodies; monitor for infection; check baseline PPD</td>
</tr>
<tr>
<td>Certolizumab pegol (Cimzia)</td>
<td>400 mg SC at 0, 2, and 4 wk; then 200 mg every other week</td>
<td>Monoclonal antibody against TNF; may have best response when used in combination with methotrexate Monitor for infections</td>
</tr>
<tr>
<td>Golimumab (Simponi)</td>
<td>50 mg SC every month</td>
<td>Monoclonal antibody against TNF Intended for use in combination with methotrexate Monitor for infections</td>
</tr>
<tr>
<td><strong>Non-TNF Biologics</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abatacept (Orencia)</td>
<td>Weight-based dose at 0, 2 and 4 wk; then monthly (i.e., 750 mg for those weighing 60–100 kg)</td>
<td>Inhibit interactions between antigens and T cells; may be useful in those who do not respond to TNF inhibitors; monitor for infusion reactions</td>
</tr>
<tr>
<td>Anakinra (Kineret)</td>
<td>100 mg SC daily</td>
<td>IL-1 receptor antagonist; avoid combination therapy with TNF agents because of elevated risk of infection</td>
</tr>
<tr>
<td>Rituximab (Rituxan)</td>
<td>Two infusions of 1000 mg given 2 wk apart</td>
<td>Chimeric antibody to CD20 protein on B lymphocytes; corticosteroid infusions help reduce infusion reactions; used in combination with methotrexate to improve response</td>
</tr>
<tr>
<td>Tocilizumab (Actemra)</td>
<td>4 mg/kg IV infusion every 4 wk; can increase to 8 mg/kg on the basis of clinical response</td>
<td>Anti–human IL-6 receptor monoclonal antibody; indicated for patients who have not responded to TNF inhibitors Monitor for infections</td>
</tr>
<tr>
<td><strong>Kinase Inhibitor</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tofacitinib (Xeljanz)</td>
<td>5 mg twice daily</td>
<td>Oral Janus kinase inhibitor; intended as second-line therapy Can be used as monotherapy or in combination with methotrexate</td>
</tr>
</tbody>
</table>

DMARD = disease-modifying antirheumatic drug; IL = interleukin; IV = intravenous(ly); NSAID = nonsteroidal anti-inflammatory drug; PPD = purified protein derivative; RA = rheumatoid arthritis; SC = subcutaneous(ly); TNF = tumor necrosis factor.
4. Malignancy is more common, particularly GI cancers and lymphoproliferative disorders. In addition, melanoma and lung cancer rates were elevated in one cohort study. Use DMARDs over biologics in melanoma; use rituximab over TNF inhibitors in lymphoproliferative disorders.

5. Osteoporosis is more common in patients with RA. Calcium and vitamin D are recommended. In addition, bisphosphonates should be considered for prevention if prednisone 5 mg or more daily is prescribed.

Patient Case

16. A 65-year-old woman received a diagnosis of RA 1 year ago. At that time, her RF titer was 1:64; she presented with joint inflammation in both hands and about 45 minutes of morning stiffness. She began therapy with oral methotrexate and currently receives methotrexate 15 mg weekly, folic acid 2 mg daily, ibuprofen 800 mg three times daily, and omeprazole 20 mg daily. At today’s clinic visit, the patient reports the recurrence of her symptoms. Radiographic evaluation of her hand joints reveals progression of joint space narrowing and bone erosion. Which is the next best step for treating this patient’s RA?

A. Administer etanercept.
B. Change to leflunomide.
C. Add prednisone bridge therapy.
D. Change to hydroxychloroquine.

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REFERENCES

Principles to Promote Optimal Medication Use in Older Adults


Dementia


Behavioral Symptoms of Dementia


Urinary Incontinence and Benign Prostatic Hypertrophy


Osteoarthritis and Rheumatoid Arthritis


1. Answer: D
Renal elimination is usually the most significantly changed pharmacokinetic value in older adults. This patient’s advanced age and diseases will add to her loss of renal function. Using the Cockcroft-Gault equation, this patient’s estimated CrCl is 24 mL/minute/1.73 m².

\[
\text{Creatinine clearance} = \frac{[(140 - 85) \times 65]}{[(72 \times 1.8)]} \times 0.85.
\]

At this level of function, glyburide elimination would be prolonged, and metformin use is contraindicated (Answer D is correct). The aspirin is low dose, and melatonin is safe even at very high doses (Answer A is incorrect). Although lisinopril is renally eliminated, dosing is based on response, and meclizine has mostly hepatic metabolism with no dosage adjustment in renal insufficiency (Answer B is incorrect). Answer C is incorrect because lisinopril, unlike glyburide, is not considered potentially inappropriate in older adults.

2. Answer: B
Common pharmacodynamic changes associated with aging include impaired homeostasis for electrolytes with angiotensin-converting enzyme inhibitors such as lisinopril and increased sensitivity to anticholinergic adverse effects from drugs such as meclizine (Answer B is correct). Lisinopril, metformin, and glyburide have primarily pharmacokinetic problems because of renal excretion changes when used in older adults (Answers C and D are incorrect). Melatonin is extremely safe without pharmacodynamic or pharmacokinetic issues in older adults, and the aspirin is low dose, so issues with GI bleeding are less than with higher doses (Answer A is incorrect).

3. Answer: A
Metoprolol, glipizide, and simvastatin are not listed in the 2015 AGS Beers Criteria tables (Answer B is incorrect). In addition to metoprolol not being listed, the patient’s CrCl is greater than 30 mL/minute/1.73 m², and nitrofurantoin is not for long-term suppression of bacteria (Answer C is incorrect). Although histamine-2 receptor antagonists are listed for patients with dementia, neither metoprolol nor clopidogrel is listed (Answer D is incorrect). However, paroxetine should be used with caution in patients with hyponatremia; ranitidine is a histamine-2 receptor antagonist, which should be avoided in patients with dementia, and this patient’s CrCl is less than 50 mL/minute/1.73 m², requiring a dose reduction; donepezil as a CI should be avoided in patients with syncope because it can cause bradycardia; and tolterodine has strong anticholinergic properties and should be avoided in patients with dementia (Answer A is correct).

4. Answer: B
Fluticasone/salmeterol meets the 10 criteria for the Medication Appropriateness Index (Answer A is incorrect). Ranitidine has no listed indication in this patient, clopidogrel has exceeded the recommended therapy duration for her stent, and metoprolol has a significant drug-drug interaction with donepezil, given her bradycardia (Answer B is correct). Aspirin is indicated because preventive therapy meets the other nine criteria of the Medication Appropriateness Index (Answer C is incorrect). Nitrofurantoin has been initiated for a presumptive urinary tract infection, given her history of frequent urinary tract infections, and simvastatin is appropriate for her disease and condition (Answer D is incorrect).

5. Answer: C
Because the patient’s A1C is less than 7.5%, glipizide should be reevaluated; donepezil use in dementia requires periodic reassessment of risk-benefit; and asymptomatic bacteriuria should not be treated with antimicrobials; these medications should be evaluated for continued need and possible discontinuation, according to the Choosing Wisely criteria (Answer C is correct). Paroxetine, ranitidine, and tolterodine are not addressed by these criteria (Answer A is incorrect). Similarly, metoprolol, clopidogrel, and tolterodine are not addressed by these criteria (Answers B and D are incorrect).

6. Answer: D
This patient had a geriatric syndrome (a fall) and hazards of hospitalization (decline in organ systems and function) that occur with many older adult patients. At this time, she has several risk factors for another fall, including a history of falls, diseases such as diabetes and hypertension, dizziness, and use of several drugs. An assessment of gait and balance would help determine the severity of her risk (Answer D is correct). Although the IADL assessment is overall good and functional, it does not focus on the risks associated with increased
falls (Answer A is incorrect). Evaluating the presence or severity of depression or of pressure sores would not be a functional assessment, though it would affect functional abilities (Answers B and C are incorrect).

7. **Answer: C**
Efforts to maintain bone and muscle strength are more important for this patient than is primary prevention of cardiovascular disease with simvastatin or lisinopril. Most older adults do not consume a diet rich in vitamin D; moreover, most older adults have less sun exposure and are more likely to be deficient in vitamin D, which is a risk factor for falls and reduced muscle strength. Furthermore, naproxen is not a good alternative for the patient because of increased risk of GI bleeding and worsening renal function (Answer C is correct). Although simvastatin and lisinopril can prevent complications caused by cardiovascular disease after extended use, they do not improve functional abilities in the short term (Answers A and B are incorrect). Pain management is important for functional status, but use of opioids compared with non-opioids has not been associated with differences in functional status (Answer D is incorrect).

8. **Answer: B**
This patient has a positive screen for mild dementia. However, when evaluating her cognitive loss, it is important to limit the use of any drug that could contribute to confusion, such as those identified on the AGS Beers Criteria, before treating for an unconfirmed condition (Answer A is incorrect). Anticholinergics such as tolterodine can cause confusion, so it would be best to discontinue this agent and reassess cognition before initiating vitamin B12 injections, the patient should have laboratory evidence of deficiency (Answer C is incorrect). Without a serum sodium concentration, there is no reason to expect that hydrochlorothiazide would cause her cognitive decline, so changing to lisinopril is not indicated at this time (Answer D is incorrect).

9. **Answer: B**
Rivastigmine is a potent inhibitor of acetyl and butyryl cholinesterase, leading to significant cholinergic adverse effects such as nausea, vomiting, and diarrhea. However, use of the transdermal delivery system generates even plasma concentrations and lessens the incidence of cholinergic adverse effects. Because the maintenance dose has been achieved with rivastigmine 12 mg, this patient can change to the patch that delivers 9.5 mg/day (Answer B is correct). Antacids will not substantially alleviate the GI effects of CIs, and prochlorperazine is anticholinergic (Answers A and D are incorrect). Because rivastigmine appears to work, it is better to continue its use, if possible, than to change to memantine (Answer C is incorrect).

10. **Answer: B**
Over 3 years, this patient’s MMSE score has decreased only 4 points, which suggests a treatment response to donepezil. Furthermore, the patient can still live at home with her husband, and she has maintained some function in her basic ADLs. However, she has not responded to a higher donepezil dose, and there is no evidence that retrying it later is useful (Answer A is incorrect). Changing from one CI to another is not effective (Answer D is incorrect). Because she has benefited from donepezil use, she should not abruptly discontinue it. Some clinical trials with memantine show an additional treatment response when memantine is added to donepezil therapy. When the benefits, risks, and costs have been openly discussed and the family prefers to consent to therapy, a time-based trial is reasonable. Memantine should be initiated at 5 mg daily (Answer B is correct). Donepezil can be evaluated for tapering after memantine titration. Vitamin E has shown no effect in most large prospective trials of AD and is not first choice to provide benefit (Answer C is incorrect).

11. **Answer: C**
Patients in the late stages of dementia (as evidenced by an MMSE score of 5/30) with behavior issues would benefit most from nonpharmacologic treatment such as music therapy (Answer C is correct). Social isolation would likely increase symptomatology, and haloperidol is not recommended until nonpharmacologic treatments have failed or patients have become a harm to themselves or others. In addition, the haloperidol dose is excessive, with risk outweighing benefit (Answers B and D are incorrect). Although pain control may be useful, ibuprofen is not the first drug of choice and has more risk of harm than benefit in a frail older adult patient (Answer A is incorrect).
12. Answer: C
Increasing the dose of a CI has not been shown to reduce agitation with dementia (Answer A is incorrect). The patient has become a harm to self (because of refusing care), so a course of quetiapine is appropriate, assuming other nonpharmacologic treatments have been tried unsuccessfully (Answer C is correct). Citalopram has small studies showing evidence of effectiveness in the literature, but its role in therapy for agitation is unclear (Answer D is incorrect). No sleep disturbance is noted, so melatonin is unlikely to help (Answer B is incorrect).

13. Answer: C
This patient has symptoms of urge incontinence. Pelvic floor exercises in conjunction with drug therapy should be offered for initial therapy (Answer C is correct). Darifenacin alone is not the best treatment (Answer B is incorrect). Some evidence indicates that solifenacin, a selective muscarinic blocker, does not worsen cognition, and solifenacin would be preferred to tolterodine in this patient with MCI (Answer D is incorrect). Mirabegron, a newer agent with less evidence for its exact role in therapy, should not be offered without pelvic floor exercises (Answer A is incorrect).

14. Answer: C
Pharmacologic therapy targeted at reducing urethral sphincter pressure has proved effective in reducing BPH symptoms. Tamsulosin is an α-adrenergic blocker with more specific activity for the genitourinary system. Given that the patient already has low normal blood pressure, tamsulosin would be preferred to terazosin (Answer C is correct; Answer A is incorrect). Orthostatic hypotension can still occur with all α-adrenergic blockers, so patients should be monitored when therapy is initiated. Finasteride, a 5-α-reductase inhibitor, and combination therapy with 5-α-reductase inhibitors are recommended when there is evidence of large prostate (Answer D is incorrect). Saw palmetto is not recommended in combination with 5-α-reductase inhibitors because it may reduce their efficacy (Answer B is incorrect).

15. Answer: B
The AGS recommends opioids for OA when older patients do not respond to initial therapy with acetaminophen (Answer B is correct). The NSAIDs and COX-2 inhibitors are seldom considered when a thorough assessment of the patient reveals that the risk of treatment (GI bleeding and worsening renal function) does not outweigh the potential benefit (Answers A and C are incorrect). Glucosamine can be added to this patient’s medication regimen; however, even if effective, it will not provide immediate pain relief (Answer D is incorrect).

16. Answer: A
This woman has indicators of a poor prognosis with RA (positive RF, many symptoms) and has not responded to methotrexate therapy. Although the next treatment step is not entirely clear, her best choices are between double- or triple-combination DMARD therapy and a biologic agent. Leflunomide or hydroxychloroquine would not be recommended as monotherapy for someone who has not responded to methotrexate (Answers B and D are incorrect). Etanercept has a response in 60%–75% of patients whose therapy with methotrexate has failed (Answer A is correct). Glucocorticosteroids are used as adjunctive therapy for the first several months of treatment with a disease-modifying agent and would be inadequate at this time (Answer C is incorrect).
ANSWERS AND EXPLANATIONS TO SELF-ASSESSMENT QUESTIONS

1. **Answer: A**
Diazepam is a long-acting benzodiazepine that can accumulate in older patients, resulting in excessive lethargy, sedation, and unsteady gait, and the patient admits taking it every night during the past week (Answer A is correct). A worsening of the patient’s depression is evident with the recent bereavement; however, that would not explain the unsteady gait (Answer D is incorrect). Lisinopril is not likely to cause this problem with his blood pressure at target, and atorvastatin is not a common cause of lethargy and confusion (Answers B and C are incorrect).

2. **Answer: C**
In older patients, the volume of distribution of lipidsoluble drugs such as diazepam is increased, not decreased (Answer D is incorrect). In addition, changes in metabolism through phase I (oxidation) are diminished (Answer C is correct). Diazepam tends to accumulate with reduced capacity for elimination, resulting in excessive sedation and an increased risk of falls in older patients. Oral absorption is not significantly altered in older adults for chronic medications (Answer A is incorrect). Decreased renal excretion is likely but is not a significant contributor in this patient, given the drugs on his medication list (Answer B is incorrect).

3. **Answer: B**
The patient has no symptoms of hypotension; therefore, no changes in her metoprolol therapy are warranted (Answer C is incorrect). Insufficient information is provided to determine the need to add memantine at this time (Answer A is incorrect). Adding vitamin D to this resident’s regimen, given her deficient serum concentrations, may help reduce falls (Answer B is correct). Adding calcium carbonate might help reduce fractures but would not reduce fall risk (Answer D is incorrect).

4. **Answer: A**
The U.S. Preventive Services Task Force recommends aspirin use in women 55–79 years of age to prevent ischemic strokes in women with a low risk of GI bleeding. This patient, who has no history of GI bleeding, would probably benefit from low-dose aspirin (Answer A is correct). Increasing the metoprolol dose or adding hydrochlorothiazide might increase the risk of falls without providing additional risk reduction at her current blood pressure (Answers C and D are incorrect). Similarly, increasing her atorvastatin dose might marginally improve her low-density lipoprotein cholesterol but would not significantly change her risk of ischemic stroke. Furthermore, because this patient is older than 75, the newest guidelines for preventing cardiovascular disease do not recommend titration above moderate-intensity statin therapy (Answer B is incorrect).

5. **Answer: B**
An initial trial of acetaminophen at doses less than 3 g/day is reasonable for frail patients with OA pain (Answer B is correct). Ibuprofen and tramadol would be alternatives when more conservative medications have failed a trial of 1–2 weeks (Answers A and C are incorrect). As-needed hydrocodone/acetaminophen should be used cautiously in older patients who have significant osteoarthritic pain and cannot tolerate other drugs (Answer D is incorrect).

6. **Answer: D**
All CIs have similar efficacy. The rivastigmine transdermal patch is better tolerated than the oral dosage formulation. Donepezil tends to be better tolerated than the other oral CIs. Doses of cholinesterase medications should be titrated slowly to prevent GI upset. The initial donepezil dose is 5 mg daily at bedtime, and for galantamine ER, the dose is 8 mg once daily (Answers A and B are incorrect). The rivastigmine patch 4.6 mg is the appropriate initial starting dose (Answer D is correct). Memantine has no beneficial effect in maintaining cognitive function, as measured by MMSE scores (Answer C is incorrect).

7. **Answer: A**
This patient’s current fasting blood glucose of 65 mg/dL and A1C of 5.6% should prompt the pharmacist to request glipizide discontinuation (Answer A is correct). The recommended A1C goal for older patients with several comorbid conditions is above 7.5%. The goals of therapy are to prevent hypoglycemia in older patients at greatest risk of this adverse drug reaction. There is no rationale for reducing the carvedilol dose, and given her normal basic metabolic panel and blood pressure, reducing potassium chloride or discontinuing lisinopril is not indicated at this time (Answers B–D are incorrect).
8. **Answer: D**
No evidence at this time supports increasing the donepezil dose to 23 mg to manage behavioral symptoms of dementia (Answer C is incorrect). The off-label use of atypical antipsychotic medications in patients with behavioral symptoms of dementia should be reserved for patients who pose a danger to themselves or others or experience hallucinations or delusions that are stressful to them (Answers A and B are incorrect). Adding acetaminophen to treat possible pain that could be causing the patient’s behavior should be tried before more aggressive strategies (Answer D is correct).

9. **Answer: A**
Any new symptom of UI in an older adult should be thoroughly evaluated to determine whether there is a reversible cause. Infection, or the “I” in the mnemonic DRIP, may be the cause of the new symptoms in this patient. Urinalysis would be the most appropriate intervention for this reversible cause of incontinence (Answer A is correct). Tolterodine is used in urge incontinence that does not respond to an adequate pelvic floor muscle trial (Answer C is incorrect). Duloxetine has been used off-label for stress incontinence (Answer D is incorrect). Pelvic floor muscle exercises or Kegel exercises should be first-line therapy for stress, urge, or mixed incontinence in women (Answer B is incorrect).

10. **Answer: C**
In this patient with comorbid conditions of hypertension and BPH, the choice of α-blockers is based on the adverse effect profiles. This patient has an elevated PVR volume, so changing tamsulosin to terazosin might reduce both blood pressure and urinary retention; merely changing to another selective α-blocker might not provide adequate relief of both conditions. (Answer C is correct; Answer A is incorrect). Increasing the atenolol dose would address only the increased blood pressure, without affecting the current problem of acute urinary retention (Answer B is incorrect). The patient is receiving moderate doses of controlled-release opioid, so reducing the hydromorphone dose for breakthrough pain is unlikely to help reduce the obstruction that may be worsened by the narcotics (Answer D is incorrect).

11. **Answer: C**
This patient is receiving 3 g of acetaminophen daily without adequate response, so a change in treatment is indicated. Diclofenac gel may provide adequate relief without systemic adverse effects (Answer C is correct). The patient, who has a history of gastroesophageal reflux disease, is taking aspirin, so naproxen is not preferred (Answer B is incorrect). Evidence indicates that initially GI bleeding is reduced with celecoxib, but this is not maintained with chronic use (Answer A is incorrect). Methylprednisolone injection is more aggressive treatment and may be considered if topical diclofenac is ineffective (Answer D is incorrect).

12. **Answer: D**
In patients with recurring RA symptoms, moderate disease activity, and the presence of a poor prognostic factor (anti–cyclic citrullinated peptides), adding sulphasalazine and hydroxychloroquine to methotrexate follows guidelines from the 2012 American College of Rheumatology recommendations update for the treatment of RA (Answer D is correct). Specifically, these guidelines recommend either double- or triple-combination DMARD therapy for patients with an inadequate response to methotrexate. Prednisone may be used as bridge therapy, but continued therapy may not be supported by a risk-benefit analysis (Answer A is incorrect). Changing methotrexate from the oral route to the intramuscular route would offer no significant benefit in this case (Answer B is incorrect). Similarly, changing methotrexate to monotherapy with leflunomide would provide no significant benefits (Answer C is incorrect).

13. **Answer: B**
Patients with a low bone mass and a T-score of –2.5 or less at the femoral neck, total hip, or lumbar spine having a 10-year probability of having a major osteoporosis-related fracture of 20% or greater according to the World Health Organization fracture risk assessment tool would benefit from an osteoporosis medication. This patient’s risk fits that category, and she already takes adequate calcium and vitamin D (Answer D is incorrect). Adding a bisphosphonate is the most appropriate intervention at this time (Answer B is correct). Adding teriparatide might be appropriate in a different scenario, such as in severe osteoporosis with a history of fracture or in the case of bisphosphonate intolerance (Answers A and C are incorrect).